JUN 10 1936

**A Hundred Years of Living, More Than Thirty Years of Planning and Twelve Years of Work Have Culminated in the Texas Centennial Exposition. There Will Be a Pharmacy Exhibit.**

Vol. XXV, No. 5 MAY, 1936

# JOURNAL

## OF THE

# AMERICAN PHARMACEUTICAL ASSOCIATION

TRADE MARK

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THE 84th ANNUAL MEETING OF THE AMERICAN PHARMACEUTICAL ASSOCIATION WILL BE HELD IN DALLAS, TEXAS, AUGUST 24–29, 1936. Hotel Adolphus, Headquarters.

Local Secretary, Walter D. Adams, Forney, Texas.

The 1936 Meetings of the American Association of Colleges of Pharmacy, the National Association of Boards of Pharmacy, Conference of Pharmaceutical Association Secretaries, of the Pharmaceutical Law Enforcement Officials and the Plant Science Seminar will also be held in Dallas, Texas.

Entered as second-class Matter, January 23, 1917, at the Post Office at Easton, Pa., under the act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in section 1103. Act of October 3, 1917; authorized July 10, 1918.

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E. F. KELLY, Secretary,
2215 Constitution Ave.,
Washington, D. C.

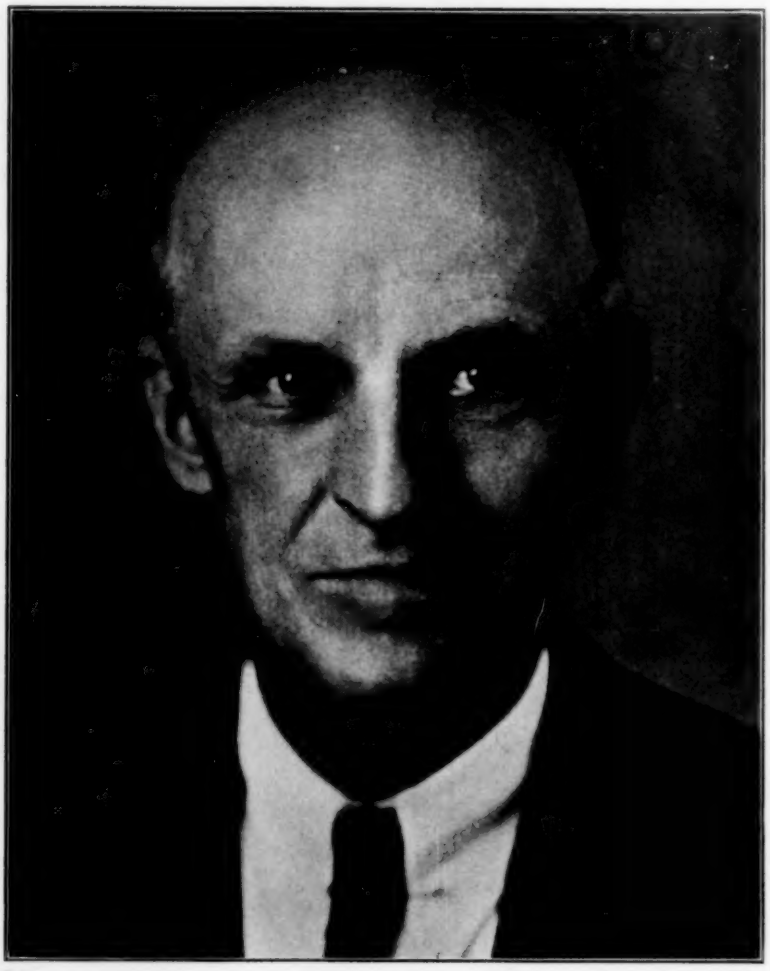
PUBLICITY FOR THE TEXAS CENTENNIAL.

The illustration shows part of the 200 Texas Centennial publicity tourists who recently visited various sections of the country. It speaks for the interest in the celebration which will open in Dallas, June 6th and close November 29th.

The photograph was taken at the Press Club Dinner in Washington. At the speakers' table is Vice-President Garner; on his right, among other notables, are Senator Connally, Post-Master General Farley, the Mayor of Dallas. On the Vice-President's left, next to the presiding officer, is the Governor of Texas. Senator Morris Sheppard is seated in front of the fourth window, Congressman Hatton Sumners is near the fifth window, Congressman Patman is in the group near the left of the picture. These statements relative to guests will have to suffice as of general interest.

The names of the members of the Transportation Committee are given on page X of the April JOURNAL; Theodore J. Bradley is the *Chairman*.

The Local Secretary of the Texas meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION is Walter D. Adams. The Local Committees will be given in another section of this issue of the JOURNAL.



ROBERT C. WILSON.

JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

VOL. XXV MAY, 1936 No. 5

## THE PRESIDENT, AMERICAN ASSOCIATION COLLEGES OF PHARMACY.

Robert Cumming Wilson was born in Sparta, Ga., October 27, 1878; here he received his early education and graduated from Sparta High School in 1896. He entered the drug business, in 1899–1902, as an apprentice in the pharmacy of Rozier and Middlebrooks, Sparta. He moved to Athens in 1902, where the young man engaged with the Orr Drug Company for a period of three years, during which time he attended the University of Georgia. In 1905, Mr. Wilson was employed in the pharmacy of H. R. Palmer & Sons, until 1907, when he entered the School of Pharmacy of the University of the South, at Sewanee, Tenn., attending the sessions of 1907–1908, during which time the student also completed two years of work in the Medical College of the same Institution. In 1908, he received from Sewanee the degree of Graduate in Pharmacy.

The School of Pharmacy of the University of Georgia, in 1907, elected Mr. Wilson instructor and he has continuously been a member of the faculty, and since 1914, dean of the School. This year he is president of the American Association of Colleges of Pharmacy.

In 1911, Professor Wilson attended the Summer School of the Medical College of the University of Michigan, specializing in Physiological Chemistry.

He was president of Georgia Pharmaceutical Association, 1913–1914, elected Secretary-Treasurer, 1929–1935, and, thereafter, Executive Secretary. In 1933–1934, he was president of the Conference of Pharmaceutical Association Secretaries.

Dean Wilson is president of the Science Club in the University of Georgia, member of the Board of Health of Athens and of Clarke County, member of the Georgia Academy of Science; member of the Association of University Professors, of Georgia Educational Association; chairman and member of various other university, chemical and pharmaceutical organizations; member of the board of directors of the Red Cross and a trustee of the First Methodist Church of Athens.

His efforts are directed to dignify pharmacy in the minds of the people and to raise educational requirements and to stimulate the efforts of professional pharmacy.

Professor Wilson married Grace Branham Troutman, October 1911; they have three children—Troutman, Grace and Robert, Jr.

# EDITORIAL

E. G. EBERLE, EDITOR 2215 Constitution Ave., WASHINGTON, D. C.

## THE U. S. P. XI AND N. F. VI OFFICIAL JUNE 1, 1936.

PHARMACISTS have had notice of the fact that the U. S. Pharmacopœia XI and National Formulary VI will replace preceding editions on June 1st. Preparations, therefore, are to be dispensed according to the new standards. Never has there been greater evidence of coöperation among the professions and the industries in the work of revision.

During 1935 many reports and other articles were published in the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION. The Abstracts of Changes will be helpful and therefore references to them are included in this comment: See page 927 in the September JOURNAL for 1934; pages 716, 784, 787, 878, 882 and 1039 of the volume for 1935.

A helpful report is that of Chairman E. Fullerton Cook in the September JOURNAL, pages 796–800, and an address by him in the February number, page 157.

The National Formulary has been freely discussed and the reports of Chairman E. N. Gathercoal will be found a helpful guide for pharmacists in shaping their work under the revised standards; the address of the Chairman before the Chicago Branch, A. PH. A., published in the February JOURNAL, beginning on page 151 will serve a useful purpose in this connection.

The discussion by Secretary Adley Nichols in the April issue, pages 344–350, presents suggestions for pharmacists that will guide them in making physicians, pharmacists and dentists better acquainted with the Formulary.

Quoting Chairman Gathercoal—"the basis of admission to the U. S. Pharmacopœia is the best drugs or medicines of known therapeutic value that are being used at the time of revision; while the basis for admission to the National Formulary is extent of usage, regardless of the consensus of the best thought of the medical profession as to therapeutic value."

The purpose of pharmacists has been to make the best and largest possible use of the standards and acquaint all who make use of them and thereby bring the professions into closer relationship for service of the public. There has been evident a coöperation of all divisions, exhibiting a spirit which will make every revision superior to the preceding.

The chairman, members of the committees and other co-workers have been loyal and earnest in their labors, representing achievement and accomplishment. The revisions reflect credit and show progress which will make possible corrections and stimulate improvement wherever these efforts may be necessary. *List of Errata* may be obtained from the chairmen or found in this issue of the JOURNAL.

## THE INFLUENCE OF PHARMACY.

PHARMACY has contributed largely to other activities through the services rendered by pharmacists; the only criticism in this connection is that often pharmacy loses all consideration. Of this there are outstanding examples: Scheele, Caventou, Pelletier, Swan and many others were pharmacists.

There are others who in their earlier years were employed in drug stores or

apprenticed in pharmacies; a number who achieved greatness, did so in the practice of medicine or in chemistry or other fields. Nevertheless there is an evident influence that remains with the individual during his life-time. This thought was prompted by the review of a book just published on "T. H. Huxley's Diary of the Voyage of H. M. S. Rattlesnake." In his early teens Huxley was apprenticed to a pharmacist, who paid him six shillings a week. His thoroughness in the pharmacy won the admiration of the doctors who loaned him books and took him to clinics. A the age of 17 he gained a free scholarship to Charing Cross Hospital; after several years of medical studies he was appointed assistant surgeon and at the age of twenty-one Dr. Huxley embarked on the Rattlesnake.

He was a student, and no great claims other than those mentioned can be given to pharmacy. "In his mind life was a sequence—the happenings of to-day were possible because of that which was done yesterday and to-morrow will be the result of to-day." "He dared to utter that which he felt was true, and the strongest desire of his soul was that he might never compromise with error for the sake of mental ease, or accept belief simply because it was pleasant."

Huxley visited the United States in 1876; he spoke at the formal opening of Johns Hopkins on "University Education" from which the following brief quotations are taken: . . . ."Again, materia, so far as it is a knowledge of drugs, is the business of the druggist. In all other callings the necessity of the division of labor is fully recognized, and it is absurd to require of the medical man that he should not avail himself of the special knowledge of those whose business it is to deal in the drugs which he uses." Other lines of the address are applicable, evidencing that Huxley remembered his drug store experience.

This experience does not call for mention, but a biographical sketch of Huxley should make reference to the fact, if for no other reason than that this apprenticeship was a sequence in his life.

Recently, Georgia had a "Crawford Williamson Long Day," three memorial celebrations marked the occasion. However much Dr. Long's discovery meant to surgery and to the afflicted, it may be questioned whether such recognition would have been possible if it had not been for the persistent efforts and loyalty of a pharmacist to his preceptor, an apprentice in "the drug shop" of Dr. C. W. Long.

"The Story of Louis Pasteur," recently, was vividly depicted by Paul Muni.

In 1851 the Société de Pharmacie de Paris offered a prize of 1500 francs for the following two problems (1) Do tartrates exist actually containing the racemic form of tartaric acid? (2) Determine the conditions under which tartaric acid might be transformed into its racemic form. Pasteur was awarded the prize; half of which he devoted toward purchasing certain necessary apparatus which lack of funds had prevented the University from acquiring for the use of his laboratory.

In 1846 Pasteur was assistant in Balard's laboratory (pharmacist). Here he prepared his thesis on "Arsenous Acids and the Arsenites of Potassium, Sodium and Ammonia." In 1849 he went to Strasbourg School of Pharmacy as Assistant Professor.

Applying Huxley: "Life is a sequence—the happenings of to-day are possible because of that which was done yesterday and to-morrow will be the result of yesterday"—Pasteur's work in pharmacy contributed largely to the achievements of a great mind.

# SCIENTIFIC SECTION

BOARD OF REVIEW OF PAPERS.—*Chairman*, F. E. Bibbins; Glenn L. Jenkins, John C. Krantz, Jr., Heber W. Youngken, L. W. Rowe, L. W. Rising, C. O. Lee, E. V. Lynn, W. G. Crockett, Frederick V. Lofgren.

## A METHOD FOR THE MEASUREMENT OF CERTAIN MECHANICAL PROPERTIES OF PHARMACEUTICAL AND TECHNICAL CREAMS.*

BY JOHN URI LLOYD, WOLFGANG OSTWALD AND HANS ERBRING.

### INTRODUCTION.

It is a generally known fact that the mechanical properties of cosmetic skin creams are widely different. Olive oil, for example, lends itself well to massage, while with lanolin, massage is practically impossible, because in the latter case the film produced on the skin is sticky instead of being smooth. Still more complicated phenomena are observed, as the senior author has pointed out, with certain skin creams in which the base consists, for example, of plant mucilages. If a small quantity of such an aqueous mucilage is put upon the back of the hand and rubbed down with the other hand, one notes at first only the sensation of wetting with water. Upon continued rubbing, however, this sensation suddenly changes to that of stickiness, and the skin, *i. e.*, the film upon it, appears pronouncedly rough. When rubbing is continued, there is again a rather sudden change; the rough skin suddenly becomes smooth again, and one has the same sensation as in rubbing soft kid leather.

This interesting observation of the complicated change which the mechanical properties of a cosmetic film undergo solely in consequence of a continuous rubbing down, formed the starting point in investigations now to be described.

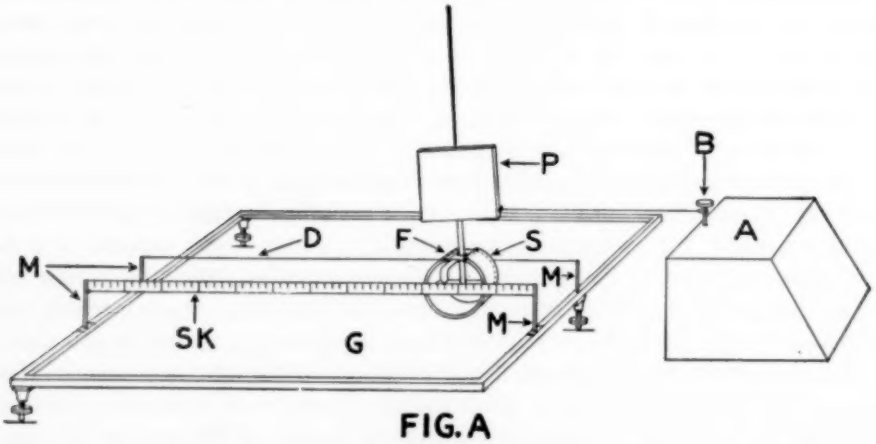



FIG. A

First of all the question arose, whether this change of the mechanical properties was merely of a subjective, or perhaps physiological nature, dependent, *e. g.*, on resorption by the living skin, or whether there are not changes in the film itself

* Translated from the German by Dr. Sigmund Waldbott.

that might be demonstrated objectively, independent of the living skin. Be it stated as one outstanding result, that the aforenamed complicated changes in the mechanical condition of such cosmetic films may in fact be demonstrated objectively, and that they are not a function of the living skin as a substrate.

DESCRIPTION OF THE APPARATUS.

The apparatus used in the subsequent experiments is illustrated in Figs. *A* and *B*.

A glass plate (Fig. *A*, *G*) is within a metal frame supported by 3 short legs which are provided with set-screws for horizontal leveling by means of a round box level. To the frame are attached at the right and the left, in each case, 2 vertical metal rods (*M*) each about 5 cm. long. One set of opposite rods is united by a metal bridge, on the front of which there is a millimeter scale (*SK*) and the other set by a very thin metal wire (*D*) drawn taut. These two metal connections serve as a guide for a sled (*S*) which can be moved to and fro between them.

The sled itself (Fig. *B*, *S*) is a short, hollow, horizontal cylinder of brass, tightly fitting into a slightly wider glass cylinder of the same length, which surrounds it except on top, where a strip of the glass is removed. An index (*Z*) at the front top edge of the sled measures its prevailing location by means of the scale.

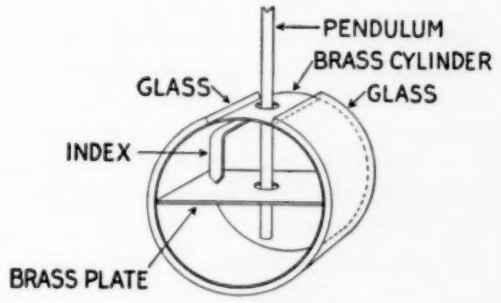


FIG.B

In the lower half of the brass cylinder there is a horizontal brass plate with a round hole in the center, exactly below another hole in the top of the brass cylinder. Through these openings passes a metal rod, *i. e.*, the end of a pendulum (*P*) about 2 m. long, having a driving weight of 10 Kg. By this arrangement, the metal rod has no rigid connection with any part of the sled, and the amount of friction of the sled against the guide connections is negligible.

When the pendulum swings, the sled is moved along, and from the character of the vibration and the character of the diminution curves (*Dämpfungskurven*), conclusions may be drawn as to the lubricating and sliding ability of the medium put between the sled and the glass plate.

In order to obtain a constant altitude of fall for the pendulum, *i. e.*, a constant driving force with which to move the sled on its base, an arresting devise (*A*) for the pendulum is installed. The pendulum is set swinging by removing a steel pin (*B*) in order that the altitude and the number of vibrations upon swinging *freely* be always the same.

With the aid of this arrangement, pure liquids and plant mucilages, emulsions and creams were examined, by observing their behavior upon friction between glass surfaces.

EXPERIMENTAL RESULTS.

*I. Pure Liquids.*—As mentioned at the beginning of this article, different plant mucilages present the phenomenon of having their gliding ability altered

with length of time of trituration. This effect, no doubt of complex nature, rendered it advisable for the purpose of seeking an explanation, first to use *pure* and *homogeneous* liquids and semi-fluid substances.

The experiments were conducted as follows:

A small portion of the substance to be examined was put upon the glass surface, and spread over the total surface involved in the rubbing. Then the rod of the pendulum was put through the holes of the sled, and the pendulum was "fixed" in place by the arresting device. Upon removing the little steel bolt, the pendulum began swinging, moving the sled with it back and forth on the glass plate. The number of vibrations, as well as the "rate of diminution" ("Dämpfung") then becomes a measure of the "gliding allowance" of the thin lubricating or sliding film between sled and glass surface.

When this sliding film has formed, we should expect that for pure systems in which mechanical manipulations cause no changes whatsoever, the "sliding ability" would be independent of the *number* and the *duration* of the sled movements, provided that the film does not evaporate. This phenomenon has indeed been clearly verified with all systems examined. The results are shown in Fig. 1.

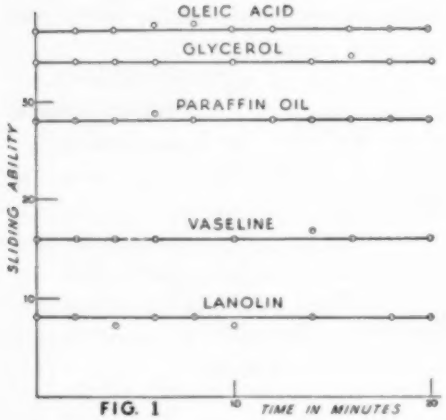


FIG. 1

The abscissæ represent times in minutes, during which the sliding ability was continuously observed. The ordinates show the (relative) sliding ability, *i. e.*, number of vibrations within a given time.

For example, with *oleic acid*, 10 consecutive experiments were carried out; the number of vibrations proved to be the same in each experiment. Similar graphic results are obtained for the other substances (systems) examined. In each case the result is a straight line (each at a different ordinate) which indicates the fact that sliding ability is a specific *constant* of the substance in question, and independent of the duration of the mechanical trituration. The figures for the "slide value" or "slide degree" of each system are given in Table I. The order in which the systems range themselves by the results of these experiments (oleic acid, glycerol, paraffin oil, vaseline, lanolin) is in accordance with experience.

TABLE I.

| Substance. | Relative Slide Degree. |
|---|---|
| Oleic acid | 37 |
| Glycerol | 34 |
| Paraffin oil | 28 |
| Vaseline | 16 |
| Lanolin | 8 |

Parallel measurements with *viscosities* of these substances show that the apparatus we use measures a distinct *sliding effect*, which does not simulate viscosities.

Thus the glycerol used gave a result in viscosity about 20% higher than the paraffin oil examined, yet the sliding effect of glycerol is considerably greater. A large number of other systems examined, demonstrated similar facts.

*II. Creams of the Type "Water in Oil."*—An essentially different picture is obtained when no longer pure systems, but *compound systems*, are investigated.

We have examined a large number of commercial pharmaceutical and cosmetic creams for their frictional or sliding capacities. First, we examined so-called "fatty creams," which represent emulsions of the type "water in oil." The graphic picture of all samples investigated, which differ but slightly one from the other in their behavior, is represented for 1 sample in Fig. 2.

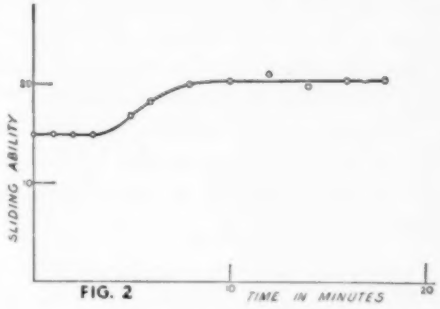


FIG. 2

A similar graph we obtained with emulsions prepared by ourselves with varying water content in vaseline or paraffin oil. We do not here need to give the different curves and figures.

At the beginning of the measurement we note at first that in each single experiment the numbers of sled movements at the same driving power until the pendulum stops swinging, remains the same. Then, however, the curve becomes more or less steep upward, that is, the sliding ability of the cream increases. When the experiments are further continued, there will again be a constant end value.

Different causes may be held responsible for this interesting increase in the sliding, lubricating or massage ability of such "water in oil" creams. First, the thought suggests itself that on account of the continued mechanical manipulation of the "emulsion film" produced, a further dispersion effect is obtained. An emulsion cream of higher dispersion perhaps has a better sliding ability than one more coarsely dispersed. However, just as well an opposite process might take place, caused by mechanical, temperature or electrical influence, *i. e.*, destruction of the emulsion in the film and a sliding of the sled finally upon the pure "fatty" surface. A more detailed examination of the effect has not yet been made; our present purpose was to find and work out a method for the examination and technical development of such creams.

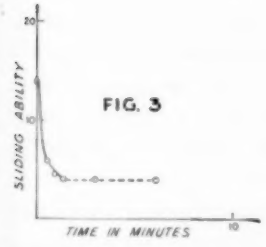


FIG. 3

*III. Creams of the Type "Oil in Water."*—Another group of systems examined by us is Creams which one might designate as "oil in water" emulsions. They are the so-called "day creams," "face creams" or "matt creams." Since in these creams the coherent (dispersing) phase is water, in which, for example, finely divided stearic acid particles are distributed in very highly dispersed form, one may expect from the start a different appearance of the sliding curves. When rubbed upon the hand, these creams show very rapidly a certain resistance, *i. e.*, the sliding ability decreases more and more during rubbing. Indeed, the same effect is obtained with our apparatus. Figure 3 shows the nature of the curves obtained with these samples. With continuous rubbing we note a steep decrease, and the manifestation of a certain end value

at a certain low sliding ability (or better, degree of "roughness"), of the stearic film produced. We suppose that in this end condition, the aqueous dispersing phase has to a large extent evaporated.

*IV. Vegetable (and Gelatin) Lotions with Glycerol.*—Undoubtedly the most interesting phenomena are obtained with by far the largest number of plant jellies. With these systems we find the complex behavior mentioned in the beginning: An intermediate stage of stickiness which makes the skin rough, and upon further rubbing the change to smoothness, whereby the skin feels like kid leather. Our apparatus illustrates objectively these different conditions which would well recommend the apparatus for examination of the mechanical properties of creams, rubbing materials, sliding materials, etc.

A commercial gelatine-glycerol jelly, showed a curve represented in Fig. 4, *i. e.*, of a nature very similar to that obtained by rubbing on the skin. The slight rise of sliding ability at the beginning of the rubbing, indicates only a *gradually*

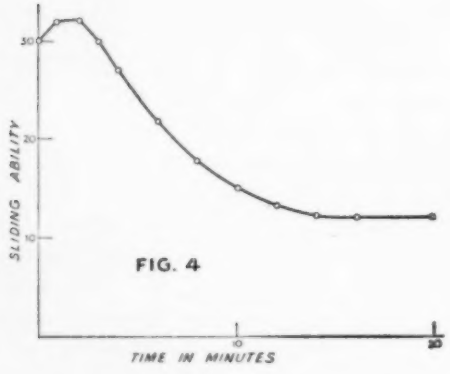


FIG. 4

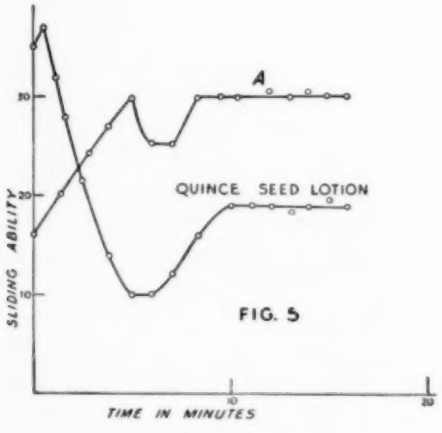


FIG. 5

intimate contact at first of the sled with the sliding material. This initial rise is especially pronounced in the following examples:

Two samples were examined: (1), a Quince seed lotion, and (2), a plant product of similar composition in American commerce. In both samples we distinctly observe the intermediate stage of "stickiness" (see Fig. 5). But we furthermore recognize that the end value of sliding ability, *i. e.*, the condition of "smoothness" in the commercial preparation, is considerably higher, *i. e.*, better, than in the Quince seed lotion.

A further plant product, a mucilage-jelly that had been obtained from flax seed was examined. Figure 6, I–III, informs us about the degrees of mechanical usefulness of this product.

After the real slide film has been formed, sliding ability decreases. The polished layer becomes rough and dull, evidently on account of decreasing water content, as in general one may perhaps be justified in associating the degree of stickiness with a definite quantity of water that happens to exist in the system. Experiments to avoid, or rather to improve this rough and dull terminal step in the gliding experiment, so undesirable in mechanical, and more so in cosmetic respect,

led to improvement of this preparation by addition of glycerol.. We observe the steady improvement of the final stage; the curve moves to higher and higher degrees of sliding ability.

GENERAL SURVEY.

The experiments herein described show that the apparatus used, gives in an excellent manner information on certain mechanical properties of Creams, Emulsions, lubricating materials, etc. No doubt this may be of some importance in

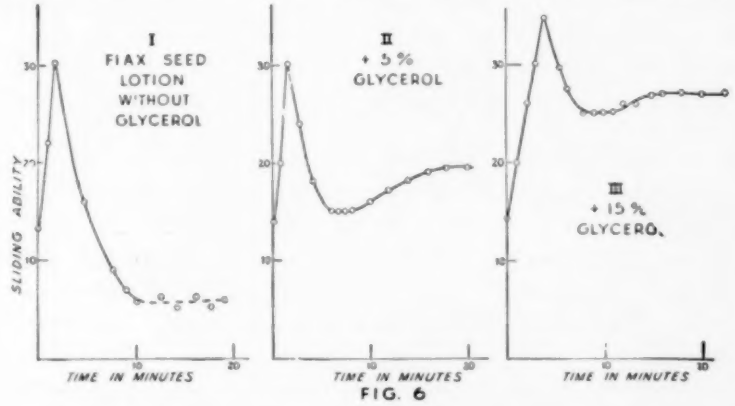


FIG. 6

technology, especially as to cosmetics. By means of it, it will be possible to get information within a few minutes concerning important mechanical properties of creams (*e. g.*, for massage purposes), objectively and reinforced by figures. Of course, besides the mechanical qualities, the specific, pharmacological and physiological effects upon the skin are of no less importance to the question of quality and adaptability of a cosmetic cream.

SUMMARY.

A method is described making it possible to characterize, objectively and numerically, the "sliding ability" of skin creams, lubricating and anti-friction materials, etc., and their very manifold and characteristic changes which take place upon continuous trituration.

A few examples of interest cosmetically are represented by curves.

---

## DRUG EXTRACTION. IX. THE EFFICIENCY OF REPERCOLATION FOR BELLADONNA ROOT AND NUX VOMICA.*,[1]

BY WILLIAM J. HUSA[2] AND C. L. HUYCK.

Although the process of repercolation has been known for many years there is practically no information in the literature giving definite data as to the efficiency of the U. S. P. X process of repercolation. The pioneer work of Squibb was con-

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cerned with the now obsolete method of saving the weak percolates from one batch of drug and placing them in storage until the next time the fluidextract was to be prepared which might be a matter of months or years. The expense of storage, the idle investment in menstrua and the possibility of deterioration during storage are the chief factors responsible for the unpopularity of this method.

The work of Diehl, which was carried out during the same period as that of Squibb, dealt with a repercolation process for half-strength fluidextracts. There was some agitation at that time for use of 50 per cent fluidextracts based on the claim that such fluidextracts could be made by the retail druggist, while the adoption of 100 per cent fluidextracts would throw the preparation of fluidextracts into the hands of the large manufacturers. However, the 50 per cent fluidextracts were not adopted and hence the work of Diehl has little application to present-day repercolation.

In later studies by Arny and Oxley (1) the repercolation process did not appear to give favorable results. This was judged from the fact the repercolation of gentian did not in most cases give a product that contained as much total extractive as did simple percolation with evaporation of the weak percolates. Scoville (2) stated that on the basis of his experience repercolation could be used with excellent results with drugs which percolated easily such as capsicum and resinous drugs in general.

As an advantage of the repercolation process, it has been stated (3) that a weak solution of the extractive of a drug is usually a better solvent for the active constituents than the original menstruum.

In order to throw some light on the exact efficiency of the U. S. P. X repercolation process, experiments have been conducted with belladonna root and nux vomica.

## EXPERIMENTAL PART.

*Fluidextract of Belladonna Root.*—Using belladonna root in No. 40 powder (assaying 0.43% alkaloids) a 1000-cc. portion of fluidextract was prepared, following the U. S. P. X directions for making fluidextracts by Type Process C (repercolation). The assays showed that 1000 cc. of finished fluidextract contained 4.6 Gm. of alkaloids and 87.7 Gm. of total extractive. These results show that repercolation was successful for belladonna root. In fact the quantity of alkaloids based on the assay of the powdered drug should have been only 4.3 Gm. This difference is probably not entirely an experimental error since in previous work it has been found (4) that extraction with the official menstruum gives slightly higher results in alkaloids than can be obtained in the official assay using ether-chloroform mixture.

In order to check up on the quantity of alkaloids in the separate reserve portions these were assayed with results as shown in Table I.

TABLE I.—ASSAY RESULTS ON RESERVE PORTIONS OF FLUIDEXTRACT OF BELLADONNA ROOT

| | Gm. Alkaloids. | Gm. Total Extractive. |
|---|---|---|
| 200 cc. reserve portion | 1.2 | 15.9 |
| 300 cc. reserve portion | 2.1 | 30.5 |
| 500 cc. reserve portion | 1.3 | 43.8 |
| Total | 4.6 | 90.2 |

Some of the experimental details of this experiment are as follows: The 500-Gm. portion of the drug was moistened with 300 cc. of menstruum; the time of percolation was 18 hours for the

reserve portion and 8, 10, 7½, 7½ and 7½, respectively, for the successive weak percolates. The 300-Gm. portion of drug was moistened with 180 cc. of weak percolate and the reserve portion was collected in 25½ hours, the time of percolation for the successive weak percolates being 5, 7, 7 and 6 hours, respectively. The 200-Gm. portion of drug was moistened with 120 cc. of weak percolate and the reserve portion was collected in 35 hours.

*Repercolation of Nux Vomica.*—Using nux vomica in No. 40 powder (assaying 2.3% alkaloids) a 1000-cc. portion of fluidextract was prepared. The U. S. P. X repercolation process was used with menstrua as follows: Menstruum I: acetic acid 100 cc., water 150 cc., alcohol 750 cc.; Menstruum II: alcohol 3 volumes, water 1 volume. Five-tenths of the acetic acid were used for the 500 Gm. portion of drug, and three-tenths and two-tenths for the 300-Gm. and 200-Gm. portions, respectively. The acid for the two latter portions was added to the first portion of weak percolate used as menstruum in each case. To keep the alcohol content the same, a volume of water equal to that of the acetic acid used for the last two portions was left out of Menstruum II. The rates of flow were as follows: 500-Gm. portion, 2 to 3 cc. per minute; 300-Gm. portion, 2 cc. per minute; 200-Gm. portion 1 to 2 cc. per minute.

The assays showed that 1000 cc. of finished fluidextract contained 21.9 Gm. of alkaloids and 128.8 Gm. of total extractive. Assays on the reserve portions are shown in Table II.

TABLE II.—ASSAY RESULTS ON RESERVE PORTIONS OF FLUIDEXTRACT OF NUX VOMICA.

| | Gm. Alkaloids. | Gm. Total Extractive. |
|---|---|---|
| 200 cc. reserve portion | 4.9 | 28.3 |
| 300 cc. reserve portion | 9.2 | 49.7 |
| 500 cc. reserve portion | 7.9 | 50.2 |
| Total | 22.0 | 128.2 |

Repercolation was fairly successful for nux vomica as 1000 cc. of fluidextract contained 22.0 Gm. of the 23.0 Gm. of alkaloids shown to be present by assay of the drug.

## SUMMARY.

Because of the lack of definite data in the literature as to the exact efficiency of the U. S. P. X repercolation process, experiments were carried out with two alkaloidal drugs. Repercolation was successful for fluidextract of belladonna root and fairly successful for fluidextract of nux vomica.

## REFERENCES.

(1) Arny and Oxley, PROC. A. PH. A., 58, 1104 (1910).
(2) Scoville, discussion of paper by Arny and Oxley, reference (1).
(3) Bennett and Cocking, "The Science and Practice of Pharmacy," Vol. I (1933), page 134.
(4) Husa and Magid, JOUR. A. PH. A., 23, 891 (1934).

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The service of pharmacy should be impressed on the public; omissions or misapplied credits are perhaps not intentional but result because the historians or biographers are not informed or do not appreciate the importance of the services rendered. Referring to Huxley—"He dared to utter that which he felt was true, and the strongest desire of his soul was that he might never compromise with error for the sake of mental ease, or accept belief simply because it was pleasant."

# PREPARATION AND TOXICITY OF BISMUTH SALTS OF CAMPHORIC ACID ESTERS.*

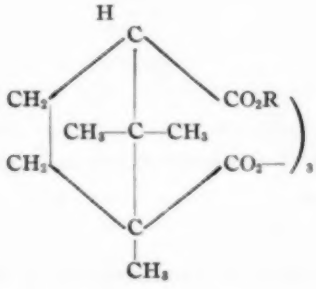
BY W. M. LAUTER AND H. A. BRAUN.[1]

The use of lipoid soluble bismuth preparations in the therapy of syphilis has increased interest in those salts of bismuth which are soluble in vegetable oils and are of low toxicity. It was in this connection that we began the investigation of three acid esters of camphoric acid and their bismuth salts.

The preparation of ortho-esters of *d*-camphoric acid has been described by Walker (1, 2), Ross and Sommerville (3), and by Edminson and Hilditch (4). We have followed Walker's (*loc. cit.*) method in preparing the ortho-methyl, ethyl and butyl esters of the acid.

Liebrecht (5) in a patent has given a general procedure for preparing bismuth salts of ortho- as well as allo-camphoric acid esters without furnishing proof of their constitution and purity. He does, however, make reference to their strongly trypanocidal action.

Walker (1, 2) and Edminson and Hilditch (4) prove that the reaction between camphoric anhydride and sodium alcoholates gives a quantitative yield of ortho-alkyl-hydrogen-camphorates, and that no allo-esters are formed. The reaction product, therefore, is in each case a neutral bismuth salt of the following constitution:




*Preparation of Bismuth-Tri-Methyl-Camphorate.*—45.5 Gm. *d*-camphoric acid anhydride are slowly added to a solution of 5.75 Gm. sodium in 290 cc. methanol. After standing for 2 hours the solution is evaporated to a volume of 90 cc. The white crystals are filtered cold and washed with a few cc. of methanol. The yield is 33.4 Gm. sodium-methyl-camphorate or 59% of the calculated yield. The material left in the methanol solution was discarded.

33.4 Gm. sodium-ortho-methyl-camphorate were dissolved in a solution composed of 100 cc. $H_2O$ and 75 cc. glycerine. 23 Gm. $Bi(NO_3).5H_2O$ were dissolved in an equal amount of the same aqueous glycerine solution. The bismuth nitrate solution was added slowly, while stirring, to the solution of the sodium salt. A white precipitate was formed. It was found that the elimination of the last traces of glycerine could only be accomplished by dissolving the product in ether, washing the ether solution with water and subsequent drying with $Na_2SO_4$.

A yield of 30.0 Gm. was obtained. The presence of some more bismuth-methyl-camphorate could be shown in the water-glycerine solution, but its recovery was not attempted. The yield is 83.6%. The melting point is 60.5–62.5° C.

The analysis is as follows: 0.3000 Gm. vacuum dried salt gave 0.904 Gm. $Bi_2S_3$ = 24.50% Bi: Calculated, 24.64% Bi.

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The solubility in vegetable oils mentioned previously by Liebrecht (5) was investigated. Oil of sweet almonds was used because of its superiority to most vegetable oils in resisting oxidizing agents.

0.7624 Gm. bismuth-ortho-methyl-camphorate was warmed with 4 cc. of oil of sweet almonds U. S. P. X, cooled and filtered. 2 cc. were analyzed for bismuth. 0.0428 Gm. $Bi_2S_3$ = 17.4 mg. Bi in 1 cc. = 7.061 Gm. bismuth-methyl-camphorate dissolved in 100 cc. room temperature saturated solution.

It was of pharmaceutical interest to determine the influence of certain compounds of therapeutic importance upon the oil solubility of this bismuth salt. It was found that oil of sweet almonds containing 0.5% anhydrous chlorbutanol by weight contained 17.60 mg. Bi per cc., or 7.142 Gm. salt in 100-cc. solution. The increase is therefore slight.

A decided and fully anticipated increase in solubility, however, was noted when 10% camphor by weight was added to oil of sweet almonds.

2 cc. of a room temperature saturated solution analyzed as follows: 0.0610 Gm. $Bi_2S_3$ = 24.8 mg. Bi per cc. = 10.07 Gm. bismuth-methyl-camphorate in 100 cc. solution.

*Preparation of Bismuth-Tri-(Ortho-Ethyl-Camphorate).*—The ethyl ester was prepared in an analogous manner by reacting sodium-ortho-ethyl-camphorate in a 50% (by weight) glycerine solution with a 50% (by weight) aqueous glycerine solution of $Bi(NO_3)_3$.

The heavy metal salt obtained is washed with water, finally dissolved in chloroform, the chloroform solution washed several times with water and finally dried with $MgSO_4$. The solvent is driven off by heating *in vacuo* for $1^1/_2$ hours at 115° C. in an oil-bath. The yield is 63.6%. The salt melts between 54° and 57° C. The analysis shows it to be a neutral salt:

Found: 23.51% Bi.

Calculated for Bi $(C_9H_4CO_2C_2H_5.CO_2)_3$: 23.47% Bi.

The salt is easily soluble in ether, acetone, chloroform, ethylene-dichloride and vegetable oils.

| Solvent. | Milligrams Bi/Cc. Metallic in a Room Temperature Saturated Solution. | Gm. Bismuth-Ethyl-Camphorate in 100 Cc. Solution at Room Temperature. |
|---|---|---|
| (1) Oil of sweet almonds, U. S. P. X | 39.5 | 16.03 |
| (2) Oil of sweet almonds + 0.5% anhydrous chlorbutanol | 41.82 | 16.97 |
| (3) Oil of sweet almonds + 10% camphor | 94.1 | 38.18 |

The influence of heat was studied by heating the salt for 16 hours at 160° C. It assumed a darker color. The product obtained was isolated by dissolving it in ethyl acetate and pouring the solution into methanol. A white salt was obtained insoluble in oil of sweet almonds and melting over a range of 204–220° C., while the bismuth-ethyl-camphorate had a melting point of 54–57° C. The analysis was as follows: 0.3000 Gm. gave 0.0954 Gm. $Bi_2S_3$ = 25.86% Bi.

It is probable that the ethyl groups have been split off because the camphoric acid molecule itself is quite stable, and without the presence of moisture there is no reason to assume the formation of a basic bismuth salt. The analysis also contradicts that. Furthermore a neutral bismuth-camphorate, prepared by reacting sodium-camphorate with $Bi(NO_3)_3$ gave a bismuth-camphorate insoluble in vegetable oils. When bismuth-ortho-ethyl-camphorate was heated at 250° C. in a 40-mm. vacuum, white crystals could be detected in the reception flask which, after

recrystallization from hot alcohol, were found to have a melting point of 220–221° C. and were identified as camphoric anhydride.

The solubility of this bismuth salt in oil of sweet almonds, U. S. P. X, was investigated and the data shown on preceding page were obtained.

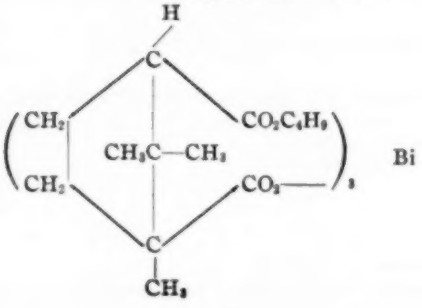
The addition of 10% camphor, as in the case of the methyl salt, increases the solubility to a considerable degree. The greater solubility of the ethyl compound compared with the methyl compound is apparent.

*Preparation of Bismuth Tri-(Ortho-n-Butyl-Camphorate).*—The sodium-ortho-*n*-butyl-hydrogen-camphorate is prepared according to Edminson and Hilditch (4) by reacting 1 mol. camphoric anhydride with 1 mol. sodium-*n*-butylate in a solution of *n*-butanol. After removing the excess butanol by evaporation *in vacuo* on a steam-bath the salt is obtained as a viscous oil, easily soluble in water.

40.5 Gm. $Bi(NO_3)_3.5H_2O$ are dissolved in a solution of 75 cc. glycerine in 100 cc. $H_2O$, and this salt solution is then added slowly, while stirring and cooling to a solution of 69.5 Gm. sodium-ortho-*n*-butyl-camphorate in 150 cc. $H_2O$ + 90 cc. glycerine. The viscous heavy precipitate is washed several times with water, then dissolved in ether, and the ether solution is washed until no more glycerine could be detected in the washings. The ether is evaporated and the residual very viscous oil is then dried *in vacuo* at 115° C. for $^1/_2$ hour. The further purification is achieved by redissolving the salt in cold methanol and precipitating it again by pouring it into water. The clear yellow oil is then washed with water, taken up again in ether and the ether solution dried with $Na_2SO_4$. The bismuth salt is now dried *in vacuo* at 100–150° C. for $1^1/_2$ hours. The yield is 65.7 Gm. = 73.5% of the calculated amount.

The analysis is as follows:

20.95% Bi found
21.38% Bi calculated for:




*Comparative Toxicity of the Camphorates.*—In these experiments, it was our object to determine the minimum lethal dose (M. L. D.) which is the dose which will kill more than 50% of the animals. The M. L. D. of the three compounds was determined on white rats weighing between 150–250 Gm. The experimental procedure consisted of injecting the three compounds individually into the leg muscles of the rat. Since the toxicity of bismuth compounds is to a large extent determined by their metallic Bi content and their rate of absorption, both of these factors were taken into consideration in our studies. The doses injected were calculated on the basis of the metallic Bi content for each preparation which for the methyl was 17.6 mg. of metallic Bi/cc., for the ethyl was 40 mg. of metallic Bi/cc. and for the butyl 43.3 mg. of metallic Bi/cc. The animals were kept under observation for thirty days.

No manifestations of irritation at the point of injection were noted on gross observation after 24 hours, 3 days, 7 days, 14 days, 21 days or 30 days. We ob-

served no indications of pain or stiffening around the point of injection. All three preparations contained small amounts of chloretone which might account for freedom from pain for a short time after injection.

Toxic symptoms with larger doses did not appear until about the sixth or eighth day after injection and death usually occurred from the fourteenth to the twenty-first day. Typical symptoms of bismuth poisoning consisting of emaciation and loss of appetite were noted.

The results of these experiments included in Table I indicate that the M. L. D. for the bismuth-methyl-camphorate is 350 mg. metallic bismuth per Kg. of rat. The bismuth-ethyl-camphorate has an M. L. D. of 250 mg. Bi/Kg. while the bismuth-butyl-camphorate is the most toxic with an M. L. D. of 150 mg. Bi/Kg. of rat.

TABLE I.—TOXICITY OF BISMUTH-CAMPHORATES IN RATS.

| Bismuth-Methyl-Camphorate. | | | | Bismuth-Ethyl-Camphorate. | | | | Bismuth-Butyl-Camphorate. | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Dose Mg. Metallic Bi/Kg. | No. of Animals. | Days Survival. | % Mortality. | Dose Mg. Metallic Bi/Kg. | No. of Animals. | Days Survival. | % Mortality. | Dose Mg. Metallic Bi/Kg. | No. of Animals. | Days Survival. | % Mortality. |
| 100 | 5 | .. | 0.0 % | 75 | 5 | .. | 0.0 % | 100 | 5 | | 0.0 % |
| 150 | 10 | 24 | 20% | 100 | 10 | 17 | 10% | 150 | 10 | 18 | 60% |
| 200 | 10 | 16 | 30% | 125 | 5 | 30 | 20% | 200 | 10 | 18 | 70% |
| 250 | 10 | 18 | 20% | 150 | 5 | .. | 0.0% | 300 | 5 | 17 | 80% |
| 300 | 20 | 12 | 30% | 200 | 10 | 15 | 30% | | | | |
| 350 | 10 | 12 | 80% | 250 | 10 | 16 | 70% | | | | |
| 400 | 5 | 6 | 100% | 300 | 10 | 15 | 80% | | | | |
| | | | | 400 | 10 | 12 | 100% | | | | |

SUMMARY.

The preparation of the ortho-methyl, ethyl and *n*-butyl esters of the bismuth salt of camphoric acid has been described and their solubility in oil was investigated.

The toxicity in oil solutions was determined by intramuscular injections into albino rats.

REFERENCES.

(1) Walker, *J. Chem. Soc.*, 61, 1088 (1892).
(2) Walker, *Ibid.*, 63, 496 (1894).
(3) Ross and Sommerville, *Ibid.*, 2770 (1926).
(4) Edminson and Hilditch, *Transactions, J. Chem. Soc.*, 225 (1910).
(5) Liebrecht, German Patent No. 461,830 (1928).

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## PREPARATION OF BENZOYL PERSULPHIDE.*

BY E. MONESS, W. A. LOTT AND W. G. CHRISTIANSEN.[1]

Some preliminary clinical results obtained by Drs. Amberg and Brunsting of the Mayo Clinic had indicated that benzoyl persulphide might prove very useful in the treatment of certain selected types of dermatosis in which pruritis was the

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predominating symptom. In order to provide sufficient quantities of this material for more extensive clinical trial the development of a satisfactory method for its preparation on a fairly large scale and in a state of high purity was undertaken.

Benzoyl persulphide has been prepared in the laboratory by many investigators in the past, and many oxidizing agents have been used for its production from salts of thiobenzoic acid. Engelhardt, Latschinoff and Malischeff (1) obtained it by treating potassium thiobenzoate in aqueous solution with a solution of iodine in potassium iodide. Weigert (2) identified a substance as thiobenzoic acid by oxidizing its sodium salt with iodine. Fromme and Schmoldt (3) precipitated benzoyl persulphide from a solution of a salt of thiobenzoic acid by means of potassium ferricyanide. Kym (4) oxidized free *p*-nitro thiobenzoic acid to the corresponding persulphide in alcoholic solution with ferric chloride. He emphasizes that only a little ferric chloride must be used; if too much is used, one obtains a gelatinous precipitate which is difficult to crystallize. For purposes of recrystallization these authors used mostly, acetone, alcohol or chloroform.

It is important that any plant process of producing benzoyl persulphide give uniform and high yields of a product which is reasonably free of impurities, and that the necessity of isolating thiobenzoic acid or its salts previous to oxidation be avoided. Furthermore, while iodine is a very suitable oxidizing agent from the chemical standpoint, it is expensive, even when a high proportion of it is subsequently recovered. It was therefore necessary to find an oxidizing agent which would be much less expensive, and which, preferably, would not involve the problem of recovery. Such an agent was found in hydrogen peroxide.

In order to explain the hydrogen peroxide process clearly it is desirable to first discuss the iodine process. An alcoholic solution of potassium hydrosulphide is prepared by saturating a solution of potassium hydroxide in absolute ethyl or methyl alcohol with hydrogen sulphide until a diluted test sample no longer gives a pink color with phenolphthalein. The reaction is:

$$KOH + H_2S \longrightarrow KSH + H_2O$$

In small scale laboratory experiments the saturation is accomplished quickly, but on a large scale, unless one tests for actual saturation there is the possibility of not quite saturating the solution. If the saturation is incomplete potassium sulphide will be present and will react in the next step in the process with benzoyl chloride to form benzoyl sulphide:

$$2\ C_6H_5\ COCl + K_2S \longrightarrow (C_6H_5CO)_2S + 2\ KCl$$

This sulphide does not yield benzoyl persulphide when treated with iodine. Therefore, the yield will be lowered in proportion to the amount of benzoyl sulphide formed from the potassium sulphide. It also serves as a source of sulphur which will contaminate the product and thereby make purification more difficult.

The alcoholic solution of potassium hydrosulphide is then treated with benzoyl chloride using one mol of the latter per two mols of the former. The chloride is added slowly with stirring and external cooling. The reaction is:

$$C_6H_5\ COCl + 2\ KSH \longrightarrow C_6H_5COSK + KCl + H_2S$$

The hydrogen sulphide is evolved and the potassium chloride precipitates. It is filtered off and washed with alcohol.

This solution is now oxidized by the addition of solid iodine in small portions, using mechanical stirring and external cooling, until a slight excess of iodine is present as indicated by a slight brownish color of the reaction mixture. During the addition of the iodine, benzoyl persulphide separates out as a fine crystalline precipitate:

$$2\ C_6H_5\ COSK + I_2 \longrightarrow [C_6H_5CO]_2\ S_2 + 2\ KI$$

The product is collected on a filter and washed with absolute alcohol. The filter cake contains beside the benzoyl persulphide also most of the iodine in the form of potassium iodide. The latter is separated from the persulphide by washing the cake with water. The extract thus obtained is a clean, water-white solution of potassium iodide, with only a minimum of organic contaminant; from this solution iodine can be recovered either as potassium iodide or as free iodine.

In order to recrystallize the benzoyl persulphide it would be quite impracticable to use acetone or alcohol or chloroform because the benzoyl persulphide is only slightly soluble in these solvents even in the hot (6–7% in hot alcohol or acetone). Tremendous volumes of solvent would be required for recrystallization. We have found that ethylene dichloride is an excellent medium from which to recrystallize benzoyl persulphide. One part of benzoyl persulphide dissolves easily in 2.5 parts of hot ethylene dichloride, and on rapid chilling of the solution a pure white crystalline substance separates out, having a melting point of 128–128.5° C.

It would appear off-hand that one mol of potassium hydrosulphide per mol of benzoyl chloride should be sufficient; this would be more economical. The reaction would yield thiobenzoic acid instead of the potassium salt.

$$C_6H_5COCl + KSH \longrightarrow C_6H_5\ COSH + KCl$$

The acid should then give the desired persulphide upon oxidation.

$$2\ C_6H_5COSH + I_2 \longrightarrow [C_6H_5CO]_2S_2 + 2\ HI$$

When this was tried experimentally the correct amount of potassium chloride separated but the yield of benzoyl persulphide was only about 50% of the theory. In addition there was obtained from the filtrate an oil, which contained no sulphur and which, after purification, boiled at 208° C.; it was found to be ethyl benzoate. The amount obtained showed that it constituted a main product of the reaction and not merely an impurity. It was also noted that though the yield of benzoyl persulphide was small, the crude product was of exceptional whiteness and purity. The conception of the reactions involved, therefore, had to be revised, and the following is the explanation of what takes place when only one mol of potassium hydrosulphide is used. Since benzoyl chloride is being added to the solution of potassium hydrosulphide, the latter is present in excess and reacts as follows:

$$C_6H_5COCl + 2\ KSH \longrightarrow C_6H_5COSK + KCl + H_2S$$

Therefore by the time half of the benzoyl chloride has been added all the potassium hydrosulphide has been used up and the second half of the benzoyl chloride reacts with the alcohol to form ethyl benzoate and hydrochloric acid. The latter reacts with the potassium thiobenzoate to produce potassium chloride and thiobenzoic acid.

$$C_6H_5COCl + C_2H_5OH = C_6H_5COOC_2H_5 + HCl$$
$$C_6H_5COSK + HCl = C_6H_5COSH + KCl$$

Combining the equations we have:

$$2\ C_6H_5COCl + 2\ KSH + C_2H_5OH = C_6H_5COSH + C_6H_5COOC_2H_5 + 2\ KCl + H_2S$$

This equation accounts completely for the quantities of products obtained: thus the quantity of potassium chloride obtained is accounted for as well as the fact that by oxidation only 50% of the quantity of benzoyl persulphide is obtained; the rest of the benzoyl chloride forms ethyl benzoate and is not available on the further oxidation with iodine. The exceptional whiteness and purity of the crude product obtained when only one mol of potassium hydrosulphide is used is attributed to the fact that thiobenzoic acid is being oxidized, whereas when two mols are used the potassium salt is being oxidized.

*Hydrogen Peroxide Process.*—In first trying to use hydrogen peroxide we prepared the solution of potassium thiobenzoate in the same manner as in the iodine process and expected the oxidation to proceed as indicated in the following reaction:

$$2\ C_6H_5\ COSK + H_2O_2 \longrightarrow [C_6H_5CO]_2S_2 + 2\ KOH$$

Benzoyl persulphide was indeed formed, but the yield was considerably less than when iodine was used as the oxidizing agent. With the latter the yield was 95–97% of the theory, whereas hydrogen peroxide under the same conditions never gave more than 60% of the theory. Furthermore the product was always contaminated with sulphur. This unsatisfactory result is due to the fact that potassium hydroxide is one of the reaction products, and alcoholic potassium hydroxide is known (3) to decompose benzoyl persulphide according to the equation:

$$[C_6H_5CO]_2S_2 + 2\ KOH = C_6H_5COSK + C_6H_5COOK + S + H_2O$$

This indicated that merely changing oxidizing agents from iodine to hydrogen peroxide does not produce a satisfactory product, and that a change in the intermediate reactions is necessary.

It will be recollected that when one mol of benzoyl chloride was allowed to react with only one mol of potassium hydrosulphide, the oxidation with iodine gave only a 50% yield of benzoyl persulphide. During the work with one mol of potassium hydrosulphide, hydrogen peroxide had been tried in place of iodine and also gave a 50% yield. In other words, the yield is the same with hydrogen peroxide as with iodine, and this 50% yield was shown to be inherent in the nature of the reactions preceding the oxidation step. Moreover, the quality of the crude product obtained using hydrogen peroxide was very high and compared favorably with that obtained using iodine. The only difference between the case in which hydrogen peroxide is used on reaction mixtures prepared with one and two mols of potassium hydrosulphide is that in the former free thiobenzoic acid is being oxidized while in the latter the potassium salt of thiobenzoic acid was being oxidized. In other words, when using hydrogen peroxide, we have in one case:

$$2\ C_6H_5COSH + H_2O_2 \longrightarrow [C_6H_5CO]_2S_2 + 2\ H_2O$$

while in the other we have:

$$2\ C_6H_5COSK + H_2O_2 \longrightarrow [C_6H_5CO]_2S_2 + 2\ KOH$$

In the second equation alcoholic potassium hydroxide is produced which partially decomposes the benzoyl persulphide while in the first equation only water and benzoyl persulphide result. It is therefore clear that in using hydrogen peroxide as the oxidizing agent we must deal with free thiobenzoic acid and not with its salts. Accordingly the following procedure was adopted: The solution of potassium hydrosulphide was prepared as before by reacting one mol of benzoyl chloride with two mols of the potassium hydrosulphide. At this point, however, instead of proceeding with the oxidation, the solution was acidified with an equivalent quantity of alcoholic hydro-

chloric acid, and the potassium chloride was filtered off and washed as usual with alcohol. This filtrate, which now contains free thiobenzoic acid in alcoholic solution was oxidized with hydrogen peroxide, and the yield was at once increased from the previous maximum of 60% to 70%. Moreover, the crude product was of a high degree of purity. The yield rose only to 70% because with alcoholic hydrochloric acid present, ethyl thiobenzoate is formed due to esterification (1). This can be avoided easily by using dilute aqueous hydrochloric acid instead of alcoholic hydrochloric acid, so that the reaction mixture was only 80% alcohol, instead of absolute alcohol. When this was done the yield at once rose to 91% of the theory, which was quite satisfactory.

## EXPERIMENTAL.

*Preparation of Benzoyl Persulphide Using Iodine as the Oxidizing Agents.*—1500 Gm. of potassium hydroxide sticks (about 85% hydroxide) are dissolved in 15 liters of absolute ethyl or methyl alcohol, and saturated with hydrogen sulphide until a diluted test sample is no longer alkaline to phenolphthalein. 1650 Gm. of benzoyl chloride are added in a thin stream from a separatory funnel with good agitation, keeping the temperature of the mixture between 10–15° C. by cooling with a freezing mixture. The separated potassium chloride is filtered off and washed with about 750 cc. of alcohol.

The filtrate and washings are cooled to 10–15° C., and 1620–1740 Gm. of solid iodine are added in small portions to the stirred solution. The temperature is preferably kept at or below 15° C. The rate of the addition of iodine is such that there is only a momentary brown color as the iodine reacts with the potassium thiobenzoate. The addition of the iodine is stopped when a permanent (a few minutes' duration) brown color appears in the reaction mixture. All through the addition of the iodine crystalline benzoyl persulphide separates out. The reaction mixture appears yellow, but after filtering off the crystalline precipitate, and washing with about two liters of alcohol, the cake appears fairly white, and there is no yellow color.

The filter cake is then washed with ten liters of water, receiving the washings in a clean vessel, and the solution is later used for iodine recovery.

The filter cake is dried in air at ordinary temperature. Yield—95% of theory calculated on the basis of benzoyl chloride.

The dried crude product is dissolved with heating on the steam-bath, using 2.5 parts of ethylene dichloride per part of product. The hot solution is filtered through a hot funnel, and chilled rapidly by means of external cooling. A fine white crystalline substance is obtained, melting point 128–128.5° C. The first crop constitutes 90% of the total crude yield.

*Recovery of Iodine.*—The aqueous washings are slightly turbid, due to a small quantity of very finely divided benzoyl persulphide. This is filtered off, and a water-white, clear solution of potassium iodide is now at hand. The potassium iodide can be crystallized out of this solution and utilized as such or the iodine recovered by saturating the acidified solution with chlorine. The recovery of iodine is 60% of the original amount used.

*Use of Hydrogen Peroxide in the Production of Benzoyl Persulphide.*—The solution of potassium hydrosulphide and of potassium thiobenzoate is prepared as usual.

Without filtering off the potassium chloride and with continuous stirring, 1200 cc. of concentrated hydrochloric acid are added in a fairly rapid drip, whereupon some additional potassium chloride precipitates. This is now filtered off and washed with two liters of alcohol, adding the washings to the filtrate. This is diluted with three liters of water at room temperature. Finally 1200 cc. of a 30% solution of hydrogen peroxide is added in a fairly rapid drip with stirring and cooling externally with cold water. When the alcoholic solution of thiobenzoic acid is oxidized with hydrogen peroxide the benzoyl persulphide does not separate at once with each increment of hydrogen peroxide, as in the case when iodine is used. It may begin to separate slowly during this addition, or it may not separate at all until all the hydrogen peroxide is added, after which most of it separates during a period of one-half to one hour. This separation is accompanied by a rise in temperature, which is kept at 30° C. or below by external cooling with water. It is easy to observe the point where the reaction is complete since the yellow reaction mixture turns milky white fairly suddenly, representing a suspension of a white crystalline substance in a water-white, clear mother liquor of alcohol. It is best to permit the mixture to stand over night in the cold, before filtering, since if the suspension were to be filtered at once, only about 83% of the yield would be obtained at this stage, the rest crystallizing from the mother liquor on standing

over night. By allowing the whole reaction mixture to stand over night we obtain the total yield with one filtration. The crude product is pure enough not to need recrystallization, but may be recrystallized once from hot ethylene dichloride if desired.

REFERENCES.

(1) *Zt. f. Chem.*, 4, 358 (1868).
(2) *Ber.*, 36, 1010 (1903).
(3) *Ber.*, 40, 2862 (1907).
(4) *Ber.*, 32, 3533, footnote (1899).

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# EVALUATION OF LIME METHODS FOR DETERMINING MORPHINE IN OPIUM.*

BY V. H. WALLINGFORD AND AUGUST H. HOMEYER.**

The literature on the determination of morphine in opium prior to 1920 was reviewed by Jermstad (1) who compared experimentally 16 official and 14 non-official methods. The early work was frequently unscientific and self-contradictory. Recent investigators have viewed the problem more critically and attempted to uncover the errors in the most widely used procedures. Hollman (2) investigated certain features of lime and ammonia methods. Reimers (3) made a critical review of the literature from 1920 to 1930.

Our research leads us to conclude that no method developed so far is satisfactory and that the precision obtainable varies with the type of opium tested. The behavior of pure morphine when subjected to many of the operations typical of lime methods has been studied in detail and the effects of various added substances have been quantitatively determined. Procedures have been devised for evaluating the errors of the principal methods now in use and the method proposed by the Commission of the League of Nations.

"Ammonia Methods" such as Jermstad's (1) are considered unsound in principle because, as pointed out by Reimers (3), the separation of narcotine from morphine by fractional precipitation with ammonia is not sharp. The lime method of the United States Pharmacopœia, Tenth Edition (U. S. P. X), the method of Dr. Joseph Rosin (4)[1] and "ammonia methods" use water to extract morphine from opium. In our experience and that of other workers (2), (5), (6), (7) this extraction is sometimes incomplete due to insufficient natural acidity of the opium.

In the methods of the United States Pharmacopœia X, British Pharmacopœia of 1932 (B. P.) and Rosin empirical aliquot parts are used which do not take into account variable factors of the opium which affect the solution. Our work has shown this practice to be inaccurate; in a particular case a U. S. P. X assay was

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* The subject matter of this paper was submitted privately to H. J. Anslinger, United States Commissioner of Narcotics, and members of the Commission of Experts of the League of Nations engaged in standardizing opium assay methods, in two progress reports dated April 2 and June 25, 1935. Acknowledgment was made in the Quarterly Bulletin of the Health Organization of the League of Nations, Vol. IV, Extract No. 16, page 816.

** Contribution from the Organic Research Laboratory of the Mallinckrodt Chemical Works, St. Louis, Mo., submitted for publication July 24, 1935.

[1] Since this paper was prepared Dr. Rosin's method has been adopted in the U. S. P. XI and becomes official on June 1, 1936.

2 per cent too high on account of this error. Recent workers (1), (2), (8), (9), (10) have recognized this source of error, and the lime method reported by van Itallie (11) for the Commission of the League of Nations (hereafter referred to as the L. N. method) provides for determination of moisture and extractibles and precise calculation of the aliquot.

Since the method reported by van Itallie is being proposed by the League of Nations as an international method, it should be pointed out that this procedure is subject to several errors inherent in all lime methods. We shall discuss these errors briefly at this point before presenting the experimental evidence on which our conclusions are based.

Morphine to the extent of 2 or 3 per cent of the total is carried down into the marc with the precipitate of calcium meconate. Our results are corroborated by Mallory and Valaer[1] who isolated similar amounts of "insoluble" morphine from thoroughly washed lime marcs by a different experimental procedure. Hollman (12) was also of the opinion that adsorption of morphine by the insoluble residue can cause a loss, and Marden and Elliott (13) observed coprecipitation of morphine with barium carbonate. Baumgarten (14) believed that practically none of the alkaloid remained in an insoluble form in the lime residue.

The assay morphine has been found to be contaminated by several per cent of titratible impurities such as by-alkaloids, calcium carbonate, etc. Baggesgaard-Rasmussen, Jackerott and Jespersen (15) found the optical rotation of L. N. assay morphine to be lower than that of the pure substance and methoxyl groups were detected by Zeisel's method. Rakshit (16) isolated 5.65 per cent benzene soluble impurities, including 3.6 per cent codeine, from B. P. assay morphine. By-alkaloids have been found in assay morphine[2] by Smith (17), Hollman (2), (12) and Jermstad (1). Marden and Elliott (13) have shown that water saturated with ether is as good a solvent for codeine as ether saturated with water. Therefore, an ether layer does not remove codeine from the water layer or prevent its coprecipitation with morphine. We have shown that lactose (and probably other substances) raises the assay[3] due, perhaps, to the formation of a titratible calcium complex. This explains in part the high results and impure assay morphine obtained by Jermstad (1) with lime methods. This error was not eliminated by extracting the assay morphine with methanol.

The solubility of morphine in the mother liquor depends in part on the kind and amount of gums, etc., present in the solution. This point was investigated carefully by Hollman (2). The correction adopted by the League of Nations Commission amounts to 28.5 mg. per 25 Gm. of lime filtrate taken in the assay, or 1.14 mg. per Gm., and is admittedly arbitrary. Our own work indicates that the solubility is 0.55 mg. per Gm. of lime solution when the starting material is pure

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[1] Private communication from Messrs. G. E. Mallory and Peter Valaer, Jr., of the Bureau of Internal Revenue, Washington, D. C. Cf. Mallory and Valaer, *Am. J. Pharm.*, 107, 515 (1935).

[2] Recently Rosin and Williams (22) reported finding about 3 per cent by-alkaloids in U. S. P. assay morphine, and that extraction with methanol eliminated approximately 2 per cent of titratible impurities.

[3] Damas (18) found that large amounts of saccharose reduced the assay.

morphine. In the case of one type of opium the solubility was found to be 16 mg. per L. N. assay or 0.66 mg. per Gm. of lime extract.

A method of purifying assay morphine published by Thoms (19) has been used by Jermstad (1) and Hollman (2), and Smith (17) described a method of determining certain impurities. For the purpose of this investigation a method was developed for purifying assay morphine by repeated precipitations under arbitrary but carefully standardized conditions. The morphine could be accounted for quantitatively by the application of a suitable solubility correction. The precision and reproducibility of the method is shown by our experimental work on pure alkaloid and assay morphine.[1] The method proved valuable in the study of lime assays and particularly in determining the purity of assay morphine when no other procedure seemed applicable. Although the process is tedious it has proved valuable in research work. Recently Mannich (20) has developed a method of determining morphine as the 2,4-dinitrophenyl ether which may prove useful.

## EXPERIMENTS ON PURE MORPHINE.

It seemed logical to investigate first the behavior of pure morphine when subjected to many of the operations typical of lime methods. The effects of various substances such as lactose, meconic acid and pseudomorphine in the lime method of assay were likewise studied using pure morphine in place of opium. The significance of these results is pointed out later in connection with the experimental data.

Since the reprecipitation procedure is repeatedly referred to in the later discussion it will be described in some detail.

*Reprecipitation of Pure Morphine.*—In Table I are given the results of reprecipitation of highly purified morphine. The samples of crystal alkaloid were weighed accurately and dissolved in a slight excess of 0.1*N* sulphuric acid and the excess titrated with 0.1*N* sodium hydroxide using methyl red indicator. The average titration of nine samples indicated 93.44% anhydrous base with an average deviation of 0.2%. The percentages given in the third column are based on the average titration.

The solutions were adjusted to the net weights indicated in the fourth column. U. S. P. alcohol and peroxide-free ether were added in the ratio of 2 cc. and 15 cc., respectively, per 30 Gm. aqueous solution. Then 1*N* ammonia was added, series A, 4 cc.; series B, 8 cc.; and series C, 11 cc. After keeping at room temperature with occasional shaking for 4 hours the samples were kept in a refrigerator at 5° C. over night. The morphine was filtered off, washed, dried, dissolved in neutral absolute methanol and titrated as in the L. N. method. The difference in mg. between the anhydrous morphine taken (based on weight and average titration) and the amount titrated after precipitation is tabulated as the loss by the first reprecipitation.

The titrated solutions were concentrated by evaporation on the steam-bath, the residual liquor was transferred quantitatively by several small portions of hot water to a flask, and the morphine was reprecipitated again under exactly the same conditions. The difference between the amounts of morphine recovered from the first and second reprecipitations is given as the loss in the second reprecipitation.

In the last column is given the percentage (based on original weights and average titration) of morphine accounted for by the final titration and a correction for solubility of 0.5 mg. per Gm. of aqueous solution.

In the working range, series A and B, the amounts of alkaloid accounted for by titration and solubility correction are in good agreement with the quantities taken. At high dilution, as in series C, a slight increase in solubility loss is indicated.

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[1] Professor R. Eder of the Institute of Pharmacy, Zürich, reported similar results by a related method to the Commission of Experts in July 1935. The information was submitted to us privately.

TABLE I.—REPRECIPITATION OF PURE MORPHINE.

| No. | Morphine Taken, Gm. (93.44% Anhydrous Alkaloid). | Morphine by Titration, %. | Aqueous Solution, Gm. | Loss by Reprecipitation, Mg. 1st. | 2nd. | % Accounted for by 0.5 Mg. per Gm. Correction. |
|---|---|---|---|---|---|---|
| A1 | 0.6000 | 99.5 | 30 | 11.6 | 14.2 | 100.7 |
| 2 | 0.6000 | 100.0 | 30 | 10.2 | 14.2 | 100.9 |
| 3 | 0.6000 | 100.2 | 30 | 13.0 | 14.3 | 100.4 |
| B1 | 1.2000 | 100.1 | 60 | 24.8 | .. | 100.5 |
| 2 | 1.2000 | 100.2 | 60 | 26.2 | 31.3 | 100.2 |
| 3 | 1.2000 | 100.3 | 60 | 23.3 | 34.2 | 100.2 |
| C1 | 1.0000 | 99.8 | 120 | 74.5 | 69.9 | 97.4 |
| 2 | 1.0000 | 99.9 | 120 | 63.2 | 75.5 | 98.0 |
| 3 | 1.0000 | 99.9 | 120 | 67.4 | 69.9 | 98.2 |

The precision of the method is borne out further by the results obtained in reprecipitating L. N. and U. S. P. assay morphine where impurities were removed by the first and second reprecipitations and no loss occurred thereafter.

*Solubility of Morphine in Mother Liquor from Lime Process.*—In order to determine the solubility of morphine in the mother liquor from lime methods two sets of experiments were made using highly purified samples of morphine alkaloid.

Three 1.2000-Gm. samples of morphine alkaloid crystals A were placed in tared flasks, dissolved in a slight excess of 0.1*N* sulphuric acid, diluted and the excess acid titrated with 0.1*N* sodium hydroxide using methyl red indicator. The solutions were adjusted to 60.0 Gm. and treated with 2 Gm. calcium hydroxide. After shaking for 1 hour the solutions were filtered and 30.0 Gm. of the filtrate (one-half aliquot) was treated with 2 cc. U. S. P. alcohol, 15 cc. peroxide free ether and 1 Gm. ammonium chloride A. R. After keeping at room temperature for 3 hours with occasional shaking and in a refrigerator at 5° C. over night, the precipitated morphine was filtered off, washed, dried, dissolved in neutral absolute methanol and titrated as in the L. N. method. The difference between one-half the original amount of morphine taken and the final amount recovered was the loss due to solubility in 30 Gm. of lime filtrate.

In a second group 1.2000-Gm. samples of crystal alkaloid B were subjected to the same procedure except that the amounts of water and all other reagents were doubled. In this case the loss due to solubility was calculated for 60 Gm. of lime filtrate.

The data are presented in Table II. In the final column is given the solubility in mg. per Gm. of lime filtrate used for precipitation.

TABLE II.—SOLUBILITY OF MORPHINE IN LIME MOTHER LIQUOR.

| No. | Morphine Taken, Gm. (by Titration). | Morphine Recovered, Gm. (by Titration). | Loss, Gm. | Solubility Mg. per Gm. |
|---|---|---|---|---|
| A1 | 1.1165 | 0.5419 | 0.0163 | 0.55 |
| 2 | 1.1166 | 0.5390 | 0.0193 | 0.64 |
| 3 | 1.1180 | 0.5405 | 0.0185 | 0.62 |
| B1 | 1.1222 | 0.5305 | 0.0306 | 0.51 |
| 2 | 1.1222 | 0.5319 | 0.0292 | 0.49 |
| 3 | 1.1208 | 0.5319 | 0.0285 | 0.48 |
| | | | Average | 0.55 |

*Effect of Dissolving Assay Morphine in Methanol.*—In order to determine the effect of drying the assay morphine and dissolving it in methanol as in the L. N. procedure two series of parallel experiments were made.

**Method I.** One-Gm. samples of pure morphine alkaloid crystals were dissolved in an equivalent amount of sulphuric acid, made up to 50 cc. in a volumetric flask and shaken thoroughly. The solution was mixed with 2 Gm. calcium hydroxide, shaken mechanically for 30–45 minutes, filtered and 25 cc. of filtrate (one-half aliquot) taken for precipitation. Two cc. U. S. P. alcohol, 15 cc. peroxide-free ether and 1 Gm. ammonium chloride A. R. were added. After shaking for 15 minutes and keeping about 18 hours at 5° C., the assay morphine was filtered off on a

3G4 sintered glass funnel, washed, dissolved in excess 0.1*N* sulphuric acid and titrated. The morphine found in 6 determinations, calculated on the basis of anhydrous alkaloid used, averaged 96.33% with an average deviation of 0.27%.

**Method II.** The above experiments were repeated with the modification of drying the assay morphine on the funnel at 100°, dissolving in neutral absolute methanol and titrating as in the L. N. method. A slight insoluble residue remained on the filter. The morphine found in three determinations averaged 94.92% with an average deviation of 0.34%. This was 1.4% lower than by Method I showing contamination of the assay morphine by basic, methanol insoluble impurities, probably calcium carbonate.

*Effect of Meconic Acid.*—By adding meconic acid to the morphine and carrying out the assay as in Method I, losses up to 3.4% were experienced probably due to coprecipitation of the alkaloid with calcium meconate which forms a gelatinous, voluminous precipitate.

TABLE III.—COPRECIPITATION OF MORPHINE WITH CALCIUM MECONATE.

Blanks by Method I Averaged 96.33% ± 0.27%.

| Meconic Acid Added, Gm. | Morphine Found (by Titration), %. | % Loss by Coprecipitation. |
|---|---|---|
| 0.5 | 92.96 | 3.4 |
| 0.5 | 93.14 | 3.2 |
| 0.2 | 92.97 | 3.3 |
| 0.2 | 94.20 | 2.1 |

*Effect of Lactose.*—Since lactose is used in diluting opium to pharmacopœia strength its effect on the assay was determined by Methods I and II.

TABLE IV.—EFFECT OF LACTOSE IN RAISING THE ASSAY.

Blanks by Method I Gave 96.33% ± 0.27%.

| Lactose Added, Gm. | Morphine Found (by Titration), %. | Increase Due to Lactose, %. |
|---|---|---|
| 0.2 | 97.60 | 1.3 |
| 0.5 | 97.77 | 1.4 |
| 0.5 | 96.89 | 0.6 |
| 1.0 | 98.26 | 2.0 |
| 1.0 | 99.91 | 3.6 |
| 1.5 | 98.85 | 2.5 |
| 2.0 | 98.91 | 2.6 |
| | Average 98.33 | 2.0 |

Blanks by Method II Gave 94.92% ± 0.34%.

| Lactose Added, Gm. | Morphine Found (by Titration), %. | Increase Due to Lactose, %. |
|---|---|---|
| 2.0 | 96.51 | 1.6 |
| 2.0 | 96.85 | 1.9 |
| 2.0 | 96.68 | 1.8 |
| | Average 96.68 | 1.8 |

The results in Table IV show that the presence of lactose raises the assay, perhaps due to formation of a basic complex with calcium which contaminates the assay morphine. The error is not avoided by dissolving the morphine in methanol. Probably other substances behave similarly.

*Oxidation and the Effect of Pseudomorphine.*—In order to determine whether morphine is oxidized appreciably in lime water by oxygen a stock solution of morphine sulphate was prepared and 50 cc. portions were assayed by Method II. The mixtures with lime were shaken and allowed to stand for various lengths of time in atmospheres of nitrogen and oxygen. As shown in Table V, it was found that no loss occurred in an atmosphere of nitrogen and the solutions remained light in color, but in an atmosphere of oxygen there was a marked loss of morphine, the solution

became dark and the precipitated alkaloid contained a dark, methanol insoluble impurity. The percentage recovered was figured on the basis of the average of the first and second determinations.

TABLE V.—OXIDATION OF MORPHINE BY OXYGEN IN LIME SOLUTION.

| Total Time in Lime, Hrs. | Time Shaken, Hrs. | Atmosphere. | Color of Solution. | Morphine Recovered, % (by Titration). |
|---|---|---|---|---|
| 0.5 | 0.5 | Air | Light | 99.9 |
| 0.5 | 0.5 | Air | Light | 100.3 |
| 24.0 | 2.0 | Nitrogen | Light | 99.9 |
| 24.0 | 2.0 | Oxygen | Dark | 90.3 |
| 24.0 | 2.0 | Oxygen | Dark | 90.3 |
| 48.0 | 2.0 | Nitrogen | Light | 100.3 |
| 48.0 | 2.0 | Oxygen | Dark | 60.3 |
| 48.0 | 2.0 | Oxygen | Dark | 63.6 |
| 48.0 | 2.0 | Oxygen | Dark | 58.8 |

It is concluded, therefore, that prolonged exposure of alkaline morphine solutions to oxygen results in loss by oxidation. The loss during an ordinary assay, where the time of exposure is less than one hour, is probably not significant.

Since pseudomorphine is the most common oxidation product of morphine, its fate in a lime assay was investigated. Pseudomorphine was prepared by oxidation of morphine with potassium ferricyanide (21). In one experiment 0.5 Gm. pseudomorphine sulphate was treated as in Method I, morphine being absent. Only a trace of precipitate was obtained by adding ammonium chloride to 25 cc. of filtered lime solution, and its titre, calculated as morphine, amounted to 26 mg. In another experiment by Method I using 1 Gm. morphine alkaloid, 0.5 Gm. pseudomorphine alkaloid was added to the lime solution. The recovery of morphine was 96.66% compared to blanks containing no pseudomorphine of 96.33%. It is concluded, therefore, that pseudomorphine contaminates the assay morphine from a lime process only to a limited extent.

### INVESTIGATION OF THE LEAGUE OF NATIONS METHOD.[1]

The sample was a mixture of Jugoslavian and Turkish opiums which lost 11.74% moisture on drying at 60–70° and was ground to pass a 50-mesh sieve.

The moisture of the ground opium was determined by drying 1-Gm. samples at 105° in an electric oven[2] (Table VI).

TABLE VI. DETERMINATION OF MOISTURE IN OPIUM.

| | Sample No. 1. | Sample No. 2. |
|---|---|---|
| Loss after 3 hours | 4.22% | 4.12% |
| Loss after 4 hours | 4.49% | 4.59% |
| Loss after 24 hours | 4.78% | 4.87% |
| Loss after 48 hours | 5.36% | 5.32% |

Extractives were determined on three occasions by the method prescribed in the L. N. method (Table VII).

TABLE VII.—DETERMINATION OF EXTRACTIVES IN OPIUM.

| | | |
|---|---|---|
| Set No. 1 | 46.1% | 46.1% |
| Set No. 2 | 44.9% | 44.6% |
| Set No. 3 | 47.0% | 47.1% |
| | Average 46.2% | |

[1] A copy of the method, dated Leyden, October 17, 1933, was received from H. J. Anslinger, United States Commissioner of Narcotics.

[2] According to Baggesgaard-Rasmussen and Co-Workers (15) the loss of weight is most reproducible by heating at 100° at 1–2 mm.

Nine determinations of morphine were made in groups of three by the method prescribed by the Commission. In order to adhere to conditions used throughout this work the precipitation was carried out by keeping the mixture at room temperature for about 4 hours with occasional shaking and then in a refrigerator at 5° C. over night. The results in Table VIII, given as per cent anhydrous morphine in the ground opium sample, were calculated by the L. N. formula, which includes a solubility correction of 28.5 mg., using 5.3% as the moisture and 46.2% as the extractives in the opium. The amount of morphine indicated by titration, calculated as anhydrous base, is tabulated in the next column.

The titrated solutions of assay morphine were saved for investigation of the purity. The amounts of extractives being known from previous determinations, all the lime extract of opium in excess of 25.0 Gm. used for precipitation of morphine was saved with the marc, acidified and worked up as described in a later paragraph. The filtered mother liquor and ether washings from the assay morphine were kept separate from washings with morphinated water, acidified and saved for determination of unprecipitated morphine.

*Purity of the Assay Morphine.*—The purity of the assay morphine was determined by reprecipitation. The titrated solutions of assay morphine, containing 5 drops excess acid, were combined in groups of three and evaporated to a small volume on the steam-bath under an electric fan. The concentrate was transferred to a tared Erlenmeyer flask and made up to 45 Gm. The transfers were made quantitatively by use of several small portions of hot water. Three cc. U. S. P. alcohol, 22.5 cc. peroxide-free ether and 5.5 cc. 1*N* ammonia were added. The process was completed as previously described under reprecipitation of pure morphine. Further reprecipitations were made in the same way. The amount of morphine accounted for by titration and solubility correction (0.5 mg. per Gm. of aqueous solution) is given in Table VIII expressed as a percentage of the original morphine indicated by titration. Experience has shown, and it is indicated by the data, that after two or three reprecipitations the assay morphine is pure and no further loss occurs in subsequent precipitations.

TABLE VIII.—PURITY OF L. N. ASSAY MORPHINE.

| No. | Results of L. N. Assays. | Morphine Isolated (Original Titration). | Purity of Isolated Morphine by Reprecipitation. 1st. | 2nd. | 3rd. | 4th. |
|---|---|---|---|---|---|---|
| 1 | 16.43% | 0.3619 Gm. | | | | |
| 2 | 16.41% | 0.3614 Gm. | 98.3% | 96.6% | 96.2% | 96.4% |
| 3 | 16.53% | 0.3642 Gm. | | | | |
| 4 | 16.31% | 0.3591 Gm. | | | | |
| 5 | 16.31% | 0.3591 Gm. | 97.5% | 96.3% | 96.0% | .. |
| 6 | 16.20% | 0.3563 Gm. | | | | |
| 7 | 16.31% | 0.3591 Gm. | | | | |
| 8 | 16.37% | 0.3605 Gm. | 97.3% | 96.3% | 96.3% | .. |
| 9 | 16.43% | 0.3619 Gm. | | | | |
| Average | 16.37% ± 0.07% | 0.3604 Gm. | | | | 96.2% |

Average amount of pure morphine isolated per assay = 0.3604 × 0.962 = 0.3467 Gm.

*Unprecipitated Morphine.*—In order to determine the amount of morphine remaining in the mother liquor, for which a correction of 28.5 mg. is allowed in the L. N. procedure, the filtrates and ether washings from the original nine L. N. assays were kept separate from the washings with morphine water, combined in groups of three and acidified with sulphuric acid. The calcium sulphate was filtered off on a sintered glass funnel and washed several times with small portions of water. The by-alkaloids were separated and the morphine isolated by applying the "shake-out" method of Stucki (8). The acid solution was extracted twice with 50 cc. portions of a 3 to 1 mixture of chloroform and isopropanol which removed some gums. The extract was washed twice with 10 cc. of 0.1*N* sulphuric acid to recover any morphine and the washings were added to the main portion. This was made alkaline to phenolphthalein with 10*N* sodium hydroxide and 2 cc. were added in excess. The by-alkaloids were extracted with 75-, 75- and 50-cc. portions of chloroform-isopropanol, the extracts being washed twice with 10 cc. of 0.1*N* sodium hydroxide and the washings returned to the main portion. Three grams ammonium sulphate were added and

the morphine was extracted with 75, 75, 75 and 50 cc. of chloroform-isopropanol. These extracts were filtered and evaporated to dryness. The residue was a dark, varnish-like gum which was dissolved in absolute methanol and titrated; a precipitate formed near the neutral point. The amounts of crude morphine found are given in Table IX.

The titrated solutions were combined, evaporated and the morphine reprecipitated from 40 Gm. of aqueous solution as described for pure morphine. The amounts of morphine accounted for (by titration and solubility) after each reprecipitation are given in Table IX.

TABLE IX.—MORPHINE UNPRECIPITATED FROM MOTHER LIQUOR.

| No. | Crude Morphine Isolated, Gm. | Pure Morphine by Reprecipitation. 1st. | 2nd. | 3rd. |
|---|---|---|---|---|
| 1–3 | 0.100 | | | |
| 4–6 | 0.093 | 0.214 Gm. | 0.177 Gm. | 0.148 Gm. |
| 7–9 | 0.100 | | | |

The precipitates from the first and second reprecipitations were deeply colored, slimy and left black residues when dissolved in absolute methanol. The final product was granular and fairly light in color. Although the precision of this determination was probably affected somewhat by the nature and amounts of impurities, the result is believed to be approximately correct. The final quantity, 0.148 Gm., was the anhydrous morphine dissolved in the mother liquors from nine L. N. assays. Therefore, the solubility per assay was 0.0164 Gm. compared to 0.0285 Gm. allowed as an arbitrary correction in the Commission's method. The amount found is equivalent to a solubility of 0.66 mg. per Gm. of aqueous solution which is in fair agreement with the loss of 0.55 mg. per Gm. suffered when pure morphine was subjected to a lime assay. As shown by Hollman (2) the presence of gums and other substances in the solution affects the solubility, so the amount of unprecipitated morphine may vary with different opium extracts.

*Morphine in the Marc.*—For the purpose of determining whether or not all morphine was in solution at the time the aliquot was taken in the L. N. method, the lime marc and all liquor in excess of the 25 Gm. used for precipitating the morphine were washed into a beaker and acidified to bromphenol blue with sulphuric acid. The volume was about 200 cc. After digesting for 1 hour at 80° it was filtered on a Büchner funnel by suction and the residue was extracted twice more with 100-cc. portions of acidified water. The quantitative isolation and purification of this morphine proved difficult, the marcs from the first six assays being used in working out a satisfactory method. It was finally accomplished by clarifying the solution by a method similar to that devised by Buchbinder[1] and removing the by-alkaloids and isolating the morphine according to the method of Stucki (8).

The acid extract, amounting to about 400 cc., was evaporated to 100 cc. and transferred quantitatively with hot water to a tared 200-cc. volumetric flask. Forty grams of powdered sodium chloride was dissolved in the liquor. The solution was neutralized with 10% sodium hydroxide and 20 cc. was added in excess. Twenty cubic centimeters saturated barium chloride solution were added. Then the flask was filled to the mark with water, shaken vigorously and weighed. The solution was filtered and 150 cc. were used for isolation of the morphine. Complete data were taken for calculation of the aliquot which was found to be 0.760 and 0.755 for two samples when precipitated solids were taken into account. The average aliquot was applied to the third sample. It is recognized that coprecipitation of morphine may occur in the clarification step, hence the amount of morphine found in the marc should be considered a minimum figure.

By-alkaloids were removed by extracting the alkaline filtrate three times with 75-cc. portions of a 3 to 1 mixture of chloroform and isopropanol. The organic layers were washed with two 10-cc. portions of 0.1*N* sodium hydroxide to recover any morphine and returned to the main aqueous layer. This was acidified with hydrochloric acid, made alkaline with ammonia and the morphine extracted with 75, 75, 50 and 50 cc. of chloroform-isopropanol. The solvent layers were filtered, evaporated to dryness and the residue dissolved in absolute methanol and titrated. The amounts of crude morphine isolated from the marcs, taking into account the aliquot, are given in Table X. The titrated solutions were evaporated together and reprecipitated as previously described. The purity, based on the original amount found by titration, is given in Table X.

[1] Private communication from the Bureau of Narcotics.

Using the data from Table X the average amount of morphine remaining in the excess liquor and marc was 0.297 × 0.883 = 0.2623 Gm.

TABLE X.—MORPHINE EXTRACTED FROM LIME MARC.

| No. | Crude Morphine in Marc. | Purity by Reprecipitation. 1st. | 2nd. | 3rd. |
|---|---|---|---|---|
| 7 | 0.302 Gm. | | | |
| 8 | 0.289 Gm. | 89.8% | 88.6% | 88.3% |
| 9 | 0.301 Gm. | | | |
| Average | 0.297 Gm. | | | |

The total amount of solution originally employed in the L. N. assay is the sum of the water, moisture in the opium and extractives:

| | |
|---|---|
| Water | 40.0 Gm. |
| Moisture in opium = 5.3% × 4 = | 0.2 Gm. |
| Extractives = 46.2% × 4 = | 1.9 Gm. |
| Total Solution | 42.1 Gm. |

Twenty-five grams of this, the aliquot, yielded 0.3467 Gm. pure morphine by precipitation and the mother liquor contained 0.0164 Gm. or a total of 0.3631 Gm. Then the excess liquor, 42.1 − 25.0 = 17.1 Gm. would contain $\frac{17.1 \times 0.3631}{25.0} = 0.2484$. Gm. Since the excess liquor and marc yielded 0.2623 Gm. pure morphine, the marc held 0.2623 − 0.2484 = 0.0139 Gm. morphine in the undissolved state, probably coprecipitated with calcium meconate. This amount, which is 2.2% of the total morphine in the opium, is in good agreement with the loss by coprecipitation (2–3%) when a solution of pure morphine and meconic acid was subjected to a lime assay.

*Check of Solubility Corrections.*—In order to check the precision of solubility corrections applied in the foregoing reprecipitations of morphine isolated from various parts of the L. N. process, the mother liquors from reprecipitation of the assay morphine and that obtained from the original L. N. mother liquors were acidified and saved.

The amounts of morphine which had been allowed were:

| | |
|---|---|
| 4 Mother Liquors from assay morphine 1–3 | 0.0900 Gm. |
| 3 Mother Liquors from assay morphine 4–6 | 0.0675 Gm. |
| 3 Mother Liquors from assay morphine 7–9 | 0.0675 Gm. |
| Morphine isolated from L. N. Mother Liquors 1–9, and mother liquors from its reprecipitation | 0.1484 Gm. |
| Total morphine allowed | 0.3734 Gm. |

These liquors were combined, made ammoniacal and extracted 4 times with 100-cc. portions of chloroform-isopropanol. The extract was concentrated to about one-half its volume and the morphine was extracted with two 50-cc. portions of 0.1*N* sodium hydroxide and washed twice more with 30 cc. of water. The combined alkaline extracts were treated with 1 Gm. ammonium sulphate to liberate the morphine which was extracted with four 100-cc. portions of the immiscible solvent. The extracts were filtered and evaporated to dryness. The residue was a black, varnish-like gum, the titration of which was only approximate due to the color of the solution. The titre indicated 0.448 Gm. morphine. The first reprecipitation accounted for 0.379 Gm. morphine and the second for 0.347 Gm. of alkaloid of good quality. This is in good agreement with the quantity (0.3734 Gm.) assumed to have been present.

*Summary of Results on League of Nations Method.*—The pure morphine found in the various parts of the L. N. assay may be summarized as follows:

| | |
|---|---|
| Precipitated from 25.0-Gm. filtrate | 0.3467 Gm. |
| Dissolved in mother liquor | 0.0164 Gm. |
| In excess liquor | 0.2484 Gm. |
| Undissolved in marc | 0.0139 Gm. |
| Total from 4 Gm. opium | 0.6254 Gm. |
| Per cent morphine in opium | 15.63 |

The difference of 0.74% between this figure and 16.37%, the average result of the original 9 assays, is made up of errors due to impurities in the assay morphine, incorrect solubility correction and coprecipitation of morphine in the lime marc.

### EXPERIMENTS ON U. S. P. X AND ROSIN METHODS.

The U. S. P. X and Rosin methods are closely related and are subject to the same inherent errors as the improved lime method proposed by the League of Nations Commission as regards coprecipitation of morphine in the lime marc and impurities in the assay morphine. No correction is applied in these methods for the solubility of morphine in the mother liquor, which is probably of the same magnitude as in the L. N. procedure. The opium is extracted (exhaustively) with water which is sometimes incomplete due to insufficient natural acidity to form salts with all alkaloids. The concentrated extract is treated with lime and an empirical aliquot is taken by volume in the U. S. P. method and by weight in the Rosin method without taking into consideration the solids precipitated by lime. This last-mentioned error and the purity of U. S. P. assay morphine have been examined experimentally.

*Precision of the Aliquot.*—Four 8-Gm. samples of opium were extracted and evaporated as in the U. S. P. X method. The concentrates were combined in a 250-cc. volumetric flask and made up to the mark. In this solution the concentration of extractives was essentially the same as in the solution used for treatment with lime in the U. S. P. X and Rosin methods.

Three-gram samples of this solution were evaporated and the residue dried at 105° to determine solids. Fifty-cubic centimeter samples were measured into tared flasks and weighed. Four grams powdered calcium hydroxide were added, the mixture shaken for 1 hour and filtered. Twenty-five-cubic centimeter portions of filtrate were measured into tared flasks and weighed. Further 3.00-Gm. samples of filtrate were evaporated and dried to determine solids. From this data, given in Table XI, the actual aliquot was calculated and compared with the empirical aliquots of the U. S. P. X and Rosin methods.

TABLE XI.—PRECISION OF EMPIRICAL ALIQUOTS.

| | Sample No. 1. | Sample No. 2. |
|---|---|---|
| (*a*) Solids from 3.00-Gm. liquor | 0.2313 Gm. | 0.2261 Gm. |
| (*b*) Wt. of 50.00-cc. liquor | 50.98 Gm. | 50.97 Gm. |
| (*c*) Wt. of 25.00-cc. lime filtrate | 25.42 Gm. | 25.44 Gm. |
| (*d*) Solids from 3.00-Gm. filtrate | 0.1646 Gm. | 0.1650 Gm. |

$$\text{Actual Aliquot} = \frac{c - d\left(\frac{c}{3}\right)}{b - a\left(\frac{b}{3}\right)} = 0.5107 \qquad 0.5101$$

Average 0.5104

$$\text{Aliquot by volume (U. S. P. X)} = \frac{25}{50} = 0.5000$$

$$\text{Aliquot by weight (Rosin)} = \frac{c}{b} = 0.4986 \qquad 0.4991$$

Average 0.4989

Therefore, the error introduced by taking the aliquot by volume would be

$$\frac{0.5104 - 0.5000}{0.5104} \times 100 = 2.04\%$$

Similarly the aliquot taken by weight would be in error 2.26%. It is evident that considerable solids were precipitated by lime, the percentage being 7.63 before and 5.49 after lime treatment.

The above experiment on precision of the aliquot was repeated on another sample of opium which yielded an extract containing 7.32% solids before and 5.81% after lime treatment. The actual aliquot was 0.5072 instead of 0.5000 as assumed in the U. S. P. X aliquot by volume. It is obvious that other opiums may contain considerably different amounts of water extractible and

lime precipitable materials. Then the magnitude of the error would be changed, but it would always raise the assay since solids are thrown out of solution by the lime.

Experiments on the empirical aliquot used in the B. P. 1932 assay showed that 52 cc. of lime filtrate represented 5.011, 5.012, 5.009, 5.012, average 5.011 Gm. opium instead of the assumed 5.000 Gm. or an error of 0.22%. It must be emphasized, however, that the error would vary markedly with moisture and extractives in the opium.

*Purity of U. S. P. Assay Morphine.*—Seven U. S. P. X assays were carried out in the official manner up to the filtration of the assay morphine. This was collected on a sintered glass funnel, washed as usual, dried at 100° and weighed. The amounts obtained were 0.700, 0.690, 0.696, 0.707, 0.672, 0.670 and 0.702 Gm. These were combined, thoroughly mixed and portions examined by the following methods.

Three 0.5-Gm. samples (Table XII) were titrated and purified by reprecipitation in the presence of alcohol and ether as previously described. Corrections were applied for loss due to solubility and the purity was calculated on the basis of the original titration.

TABLE XII.—PURITY OF U. S. P. X ASSAY MORPHINE BY REPRECIPITATION.

| Wt. Taken. | Anhydrous Morphine, Indicated by Titration, Gm. | Purity by Reprecipitation. 1st. | 2nd. |
|---|---|---|---|
| 0.5000 | 0.4663 | 94.1% | 92.1% |
| 0.5000 | 0.4677 | 94.4% | .. |
| 0.5000 | 0.4663 | 93.5% | 90.6% |

Two 1-Gm. samples were dissolved in absolute methanol as in the L. N. method and titrated. The solutions were evaporated and transferred to a separatory funnel; added 2.0 cc. 10*N* sodium hydroxide and extracted with 40-, 30- and 30-cc. portions of a 3 to 1 mixture of chloroform and isopropanol to remove by-alkaloids. The extracts were washed counter-currentwise with a little water to recover any morphine. The chloroform layers containing non-phenolic alkaloids were combined, evaporated, the residue dissolved in neutral methanol and titrated. The morphine was precipitated from the aqueous layers in the presence of alcohol and ether, determined in the usual manner, and a correction of 0.5 mg. per Gm. of solution added for solubility. The results were calculated as percentage of the original titration and are presented in Table XIII. Further loss in titratible material due to water-soluble impurities is indicated in the last column.

TABLE XIII.—IMPURITIES ACCOMPANYING U. S. P. ASSAY MORPHINE.

| Wt. Taken Gm. | Anhydrous Morphine, Indicated by Titration, Gm. | Non-Phenolic Alkaloids. | Morphine Recovered. | Water-Soluble Impurities. |
|---|---|---|---|---|
| 1.0000 | 0.9298 | 3.83% | 91.5% | 4.67% |
| 1.0000 | 0.9326 | 3.52% | 92.3% | 4.18% |

It is concluded, therefore, that the titration of U. S. P. assay morphine from this opium included 8–9% impurities of which 3.6% were non-phenolic alkaloids and 4.4% were water-soluble, basic substances.

U. S. P. assay morphine was prepared from another sample of opium and purified by reprecipitation. The purity was calculated as a percentage of the original titration (Table XIV).

TABLE XIV.—REPRECIPITATION OF U. S. P. X ASSAY MORPHINE.

| Wt. Taken Gm. | Anhydrous Morphine, Indicated by Titration, Gm. | Purity by Reprecipitation, %. 1st. | 2nd. | 3rd. |
|---|---|---|---|---|
| 1.0000 | 0.9168 | 96.8 | 96.6 | 96.6 |
| 1.0000 | 0.9154 | 97.0 | 96.8 | 96.7 |
| 1.0000 | 0.9154 | 97.5 | 96.8 | 96.8 |

In this case the assay morphine was much purer (96.7%) than that yielded by the previous sample of opium (92%) by the same assay method.

## SUMMARY AND CONCLUSIONS.

The behavior of pure morphine in a lime assay has been studied and procedures have been described for investigating methods of opium analysis. The principal lime methods, including the one proposed by the Commission of the League of Nations, have been thoroughly investigated. The sources of error, and their magnitude in particular cases, have been pointed out. It has been found that:

(*a*) Morphine is coprecipitated with calcium meconate.

(*b*) The solubility correction used in the League of Nations method is approximately double the amount of morphine that can be extracted from the mother liquor, and is double the loss suffered by pure morphine when it is substituted for opium in the assay.

(*c*) The assay morphine is contaminated by basic impurities, including byalkaloids and calcium salts.

(*d*) Substances such as lactose raise the assay.

(*e*) Empirical aliquots are inaccurate.

The errors of lime methods vary depending upon the type of opium. It has been our experience that the results are generally too high. It is concluded that the ultimate solution of the problem does not lie in the direction of lime methods.

We are now engaged in the study of methods based on extraction with immiscible solvents which we expect to make the subject of a later paper. Such methods offer many desirable features but in their present form appear to be unsatisfactory in certain details such as size of sample, the nature of the immiscible solvent and the purity of the assay morphine.

We gratefully acknowledge assistance from H. J. Anslinger, United States Commissioner of Narcotics, and Charles H. LaWall, United States representative on the Commission of Experts, who have encouraged us in this work, and from Dr. H. J. Wollner, consulting chemist, United States Treasury Department, who has made available to us reports and private communications bearing on this problem.

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## THE BIOASSAY OF VERATRUM VIRIDE.*,[1]

BY B. V. CHRISTENSEN[2] AND A. P. MCLEAN.

Although the U. S. P. X recognizes no chemical or biological assay for *Veratrum viride*, it is a well-known fact that the preparations of this drug vary greatly in potency (1, 2). This variation in potency and the lack of a satisfactory assay method seem to be the only explanation for the fact that this drug has been almost completely discarded.

A chemical assay has been suggested (3, 4), but since the activity of *Veratrum viride* is due to a number of alkaloids which differ qualitatively and quantitatively in action (5) it would appear that a chemical assay would not be sufficient. This has been pointed out by several workers (1, 6).

Houghton and Hamilton (7) reported a biological assay of *Veratrum viride* based upon the M. L. D. per Gm. body weight of frog. Pilcher (2) did further work with this method and concluded that for all practical purposes the frog assay appeared to be satisfactory.

Rowe (8), in reporting a biological assay based upon the M. L. D. for white mice, made the following comment on the indefinite end-point of the frog method and the length of time required: "A whole series of frogs given graded doses may be found fifteen hours later to be more dead than alive, but still they are not dead and even a skilled technician hesitates about drawing any conclusions." In our experience the mouse method has the same objection. The advantages claimed for the mouse method were that fewer animals were needed and that the assay required less time. Pilcher (2) used an M. L. D. for guinea pigs but preferred the frog method.

*Veratrum viride* is a centrally acting cardiac depressant. In therapeutic doses it has a selective stimulating action on the vagus nerve (9). It has long been known that large doses cause emesis. Some workers claim that the emesis is central, while some claim that it is local. Hanzlik (10) states that the emesis of Veratrum is the result of local irritation, and that it is produced by intraperitoneal but not by intravenous injections.

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* Scientific Section A. PH. A., Portland meeting, 1935.

[1] From a thesis presented in partial fulfilment of the requirements for the degree of Master of Science in Pharmacy, University of Florida, August 1935.

[2] Director of the School of Pharmacy, Head of Department of Pharmacognosy and Pharmacology, University of Florida.

Since it appears that a chemical assay for *Veratrum viride* is not sufficient, and since the biological assays presented require long periods of observation and lack definite and easily observed end-points, it is evident that a more satisfactory assay method is needed. In view of the fact that Veratrum is a medullary stimulant, that the vomiting centers are located in the medulla and that emesis usually results from the administration of large doses, it is quite probable that this emesis is a result of the central medullary stimulation, that it is a manifestation of the desired pharmacological action and that it would furnish a satisfactory basis for a biological assay. We have found that small and very definite doses of Veratrum consistently produced emesis upon intravenous injection in pigeons. We also found, in our first experiments, that we could determine the emetic dose of a tincture within a range of 0.005 cc. per Kg. body weight of pigeon. This accuracy, the fact that emesis results within only a few minutes after administration, that the technique was very simple, that the animals were not killed and could be repeatedly used, suggested this as an ideal assay method.

In this preliminary work the potencies of six tinctures of *Veratrum viride*, U. S. P. X, were compared, using the average minimum emetic dose for pigeons as the basis for comparison. Three of these, No. 102, No. 104 and No. 105, were commercial tinctures prepared by reliable manufacturers. Two of these, No. 102 and No. 104, were claimed by the manufacturer to assay 0.1 per cent total alkaloids. The other tinctures, No. 110, No. 111 and No. 112, were prepared by the U. S. P. X process from the crude drug obtained from reputable drug houses.

In order to compare the effect of the method of administration upon the emetic dose, the M. Em. D. of one tincture, No. 112, was also determined by intraperitoneal injection. The intravenous method seemed much superior and was, therefore, used with the six preparations included in this work.

*The minimum emetic dose was considered as the smallest dose, expressed in cc. of the tincture per Kg. body weight, which would produce emesis within fifteen minutes in approximately 75 per cent of the pigeons injected.*

The method used was very similar to the one proposed by Hanzlik (10) for estimating the potency of digitalis. Adult pigeons weighing, roughly, from three to four hundred grams were used. Freshly prepared dilutions (1 to 20 and 1 to 40) of the tincture in physiological salt solution were injected into the wing veins, and the pigeons placed in individual cages and observed for a period of fifteen minutes. A longer period of observation was found to be unnecessary. The emesis which resulted, usually in from two to five minutes, was of short duration and was characterized by a downward craning movement of the head and a convulsive flapping movement of the wings. There was usually an expulsion of gravel or mucus.

In determining the emetic dose for each preparation two doses of a wide range were first given to "bracket" the emetic dose, and then by a series of injections of doses within this range the minimum emetic dose was approached. Since the doses well below the emetic dose failed to produce emesis in almost every case and the doses above the emetic dose in all but one case, No. 110, caused emesis, only the emetic doses and the doses just below the emetic dose have been included in the tables.

The results obtained in determining the average minimum emetic dose of six tinctures of *Veratrum viride* intravenously, the results of one determination using

intraperitoneal injection, and a comparison of the potencies of the six tinctures based upon this method, are presented in the following tables:

TABLE I.—THE AVERAGE MINIMUM EMETIC DOSE OF SIX TINCTURES OF VERATRUM VIRIDE.

| Preparation Number. | Dose Cc./Kg. | Number of Injections. | Emesis. | No Emesis. |
|---|---|---|---|---|
| 102 | 0.060 | 7 | 1 | 6 |
| | 0.065* | 11 | 10 | 1 |
| 104 | 0.050 | 5 | 0 | 5 |
| | 0.060* | 11 | 8 | 3 |
| 105 | 0.020 | 10 | 3 | 7 |
| | 0.030* | 7 | 7 | 0 |
| 110 | 0.020 | 14 | 7 | 7 |
| | 0.025* | 5 | 5 | 0 |
| | 0.030 | 8 | 6 | 2 |
| 111 | 0.020 | 10 | 4 | 6 |
| | 0.030* | 7 | 6 | 1 |
| 112 | 0.020 | 11 | 4 | 7 |
| | 0.030* | 6 | 6 | 0 |

* Minimum Emetic Dose.

TABLE II.—A COMPARISON OF THE AVERAGE MINIMUM EMETIC DOSE OF THE SIX PREPARATIONS TESTED. ALSO, A COMPARISON OF THE POTENCIES OF THE PREPARATIONS AS INDICATED BY THE DIFFERENCE IN THE SIZE OF THE INTRAVENOUS EMETIC DOSE FOR PIGEONS.

(For Convenience of Comparison, Preparation 102 Is Indicated as Having a Potency of 100 Per Cent.)

| Preparation. | M. Emetic Dose Cc./Kg. | Comparative Potency. |
|---|---|---|
| 102 | 0.065 | 100% |
| 104 | 0.060 | 108% |
| 105 | 0.030 | 217% |
| 110 | 0.025 | 260% |
| 111 | 0.030 | 217% |
| 112 | 0.030 | 217% |

TABLE III.—THE INTRAPERITONEAL EMETIC DOSE OF PREPARATION NO. 112.

(This Is the Only Case in Which Intravenous Injection Was Not Used.)

| Dose Cc./Kg. | Number of Injections. | Emesis. | No Emesis. |
|---|---|---|---|
| 0.040 | 4 | 0 | 4 |
| 0.060* | 4 | 3 | 1 |

* Minimum Emetic Dose.

## DISCUSSION AND CONCLUSIONS.

As shown by Table II, there was a wide variation in the potencies of the tinctures tested as indicated by the difference in the size of the intravenous dose necessary to produce emesis in pigeons. Preparations No. 102 and No. 110 (Tables I and II), prepared by the U. S. P. X process, showed a variation in potency of more than 100 per cent.

Although the time required for emesis to take place was not given in the preceding tables, the average time required for emesis following intravenous injections was about five minutes. In no case did emesis occur after fifteen minutes.

For the purpose of comparing methods of administration, the minimum emetic

dose of preparation No. 112 was determined by intraperitoneal injection (Table III). It was found that approximately twice the intravenous dose (Table I) was required to produce emesis when the drug was administered by this method. It was also found that approximately twenty minutes was required for emesis to take place following intraperitoneal injections.

No attempt was made to determine the seat of the emetic action; however, the following data indicate that emesis is the result of a central action rather than the result of local irritation as claimed by Hanzlik (10): 1. Intravenous injections of the drug produce emesis usually in from two to five minutes. 2. About twenty minutes is required for an emetic action to take place when the drug is administered intraperitoneally. 3. The intravenous emetic dose is much smaller than that dose required to produce emesis when injected intraperitoneally. 4. The consistency obtained would hardly have been possible had the emetic action been due to local irritation. The fact that *Veratrum viride* is known to act upon the medullary center and that the vomiting centers are located in this part of the brain further substantiate these indications.

From the consistency obtained in this preliminary work it appears that the minimum emetic dose for pigeons might furnish a satisfactory basis for a biological assay of this drug; however, further work is being done in an attempt to definitely determine its reliability.

If it can be shown that the pigeon emesis method gives a reliable measure of the desired pharmacological activity of *Veratrum viride*, it would have the following attributes of a good biological assay method: 1. A very definite and easily recognized end-point. 2. Economy. The pigeons may be repeatedly used. 3. Little time is required. The maximum period of observation is fifteen minutes. With the frog method, which seems to be in greatest favor, this period may exceed twenty-four hours. 4. An accuracy of within 10 per cent. 5. Simplicity. The technique is very simple and does not require the aid of an assistant.

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## STORY OF LIFE AT TEXAS CENTENNIAL.

"The Story of Life," a coöperative exhibit created at a cost of $100,000.00, which will occupy more than 10,000 square feet in the great hall of the Federal Government, promises to be one of the outstanding attractions of the Texas Centennial Exposition.

Dr. E. H. Cary, former president of the American Medical Association, is coöperating with officials of the United States Public Health Service and the Smithsonian Institution. Seven of the leading universities of Texas and the medical profession of State and Nation have joined with these agencies to present the display. Pharmacists participate in the exhibit.

# PHENOLIC ESTERS OF *p*-METHOXYCINNAMIC ACID.*

BY C. W. SONDERN.

The acid used in the experiments here described was obtained from its natural ethyl ester separated from the oil of *Kampferia Galanga* L. This oil had been prepared at the Botanical Garden at Buitenzorg, Java, to the Director of which thanks are due for his kind coöperation. The oil had been distilled for the purpose of securing a somewhat larger amount of *n*-pentadecane, first isolated by van Romburgh. However, since the oil consists largely of the handsomely crystallizable ethyl ester of *p*-methoxycinnamic acid it seemed desirable to use this material for further study of its derivatives.

*Guaiacol Ester.*—The method followed was the one successfully employed by P. A. Foote (1). A mixture of 5 Gm. of acid, 3.5 Gm. of liquid guaiacol and 2.4 cc. of phosphorus trichloride in 80 cc. of anhydrous toluene was refluxed gently first in a water-bath for an hour, then in an oil-bath for another hour. The toluene having been removed by distillation under diminished pressure, the reaction product was washed with 5% aqueous KOH to remove any excess acid or phenol. The residue when recrystallized from alcohol yielded 4.5 Gm. (57% of theoretical yield computed on the acid used) of a product melting at 102–103°. Upon saponification, duplicate determinations yielded values of 181 and 188. The theoretical saponification value is 186. The acid regenerated from the saponification liquid melted at 170°, the m. p. of *p*-methoxycinnamic acid. Guaiacol was identified in the saponification liquid by means of the ferric chloride test.

*α-Naphthol Ester.*—The same process applied to α-naphthol yielded a crystalline product, but the yield was low, *viz.*, 22%. Recrystallized, it melted at 102°. Upon saponification, duplicate determinations yielded 197 and 180, respectively. The computed S. V. is 184. The regenerated acid melted at 170°. The α-naphthol recovered melted at 90°, the recorded m. p. being 94°, and gave a positive test with ferric chloride.

*Resorcinol Esters.*—An attempt to prepare resorcinyl paramethoxycinnamate using phosphorus trichloride as the condensation agent resulted in the formation of large amounts of resinous by-products. To remedy this, phosphorus pentoxide (2) was used.

(I) Three and three-tenths grams of the acid and 2.1 Gm. of resorcinol were dissolved in approximately 60 cc. of toluene together with 1.2 Gm. of phosphorus pentoxide. The mixture was refluxed on an oil-bath for two hours and then the toluene was distilled off under diminished pressure. The product was washed with 5% aqueous KOH to remove any free acid, phenol or mono-ester. The residue, crystallized from hydro-acetone solution, yielded 0.5 Gm. of a product melting at 172–173°. In order to examine this further a larger quantity of material was prepared.

(II) Five grams of *p*-methoxycinnamic acid and 3.2 Gm. of resorcinol were dissolved in approximately 80 cc. of toluene together with 2 Gm. of phosphorus pentoxide. The mixture was refluxed on an oil-bath for two hours and then the toluene was distilled off under diminished pressure. The residue in the distilling flask was washed with 5% aqueous KOH and the product removed and dried in a desiccator over $CaCl_2$. When crystallized from a hydro-acetone solution and dried, it yielded a light orange crystalline product weighing 1.51 Gm. and melting at 171–172°.

The products from the two experiments were combined and recrystallized. Yield 1.84 Gm., m. p. 173–173.5°. Duplicate saponifications on this product

* From the Laboratory of Edward Kremers, Madison, Wis.

yielded values, 259 and 256. The theoretical saponification value for the di-ester is 261. Analysis of the saponification liquor yielded *p*-methoxycinnamic acid m. p. 170° and resorcinol m. p. 115°.

An attempt was made to isolate the mono-ester from the alkaline washings obtained from the above experiments.

The alkaline solution was carefully neutralized with 10% HCl and the neutral solution extracted several times with ether in order to remove any unreacted resorcinol along with the mono-ester. When the aqueous solution was acidified a small amount of impure *p*-methoxycinnamic acid was recovered. The ether-soluble fraction was concentrated and the product dried. A few red crystals melting at 135–137° (with decomposition) were obtained. The quantity of this product was too small to permit its characterization.

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# THE ADDITION OF STRONG HYDROGEN PEROXIDE IN THE DETERMINATION OF NITROGEN IN ORGANIC COMPOUNDS.*

BY CHARLES F. POE AND BARTLETT T. DEWEY.

## INTRODUCTION.

The amount of nitrogen in some organic compounds is determined successfully by the Gunning or Kjeldahl methods. These two methods have advantages over the Dumas method because of the ease of manipulation and the use of less expensive apparatus. However, the distillation methods are subject to certain limitations because the results in the analysis of compounds containing such groups as nitro, nitroso, azo, azoxy, etc., are inconsistent. Many organic compounds also require a very long period of heating in order to liberate all of the nitrogen.

The investigation reported in this communication was undertaken in order to determine accurately the amount of time saved and the accuracy obtainable when thirty per cent hydrogen peroxide was used in the determination of nitrogen. In the last few years, a number of investigators (1–10) have found hydrogen peroxide to be a valuable oxidizing agent in the decomposition of organic substances, because it hastens the process of digestion and cuts down foaming.

## EXPERIMENTAL.

The method employed in the investigation reported in this paper was the Gunning modification of the original Kjeldahl method, which is official with the Association of Official Agricultural Chemists (11). Twenty-five hundredths gram of the organic compound was placed in each of two digestion flasks with ten Gm. of nitrogen-free potassium sulphate and twenty cc. of concentrated sulphuric acid. The contents of both flasks were digested over electrically heated plates, all units of which were of the same construction and gave the same amount of heat. During the digestion, one cc. of a 30 per cent solution of hydrogen peroxide was added to one of the flasks at intervals of ten minutes. The contents of the other flasks were allowed to digest without the addition of the hydrogen peroxide. Each sample was heated until the liquid in the flask was light

* Scientific Section, A. Ph. A., Portland meeting, 1935.

straw color. This color, in the case of the amino compounds, was found to indicate the point at which complete conversion of nitrogen into ammonium acid sulphate was effected.

In Table I are given the results of the analysis of a number of organic amino compounds. The study of the above-mentioned table demonstrates that both the Gunning method and the modification making use of strong hydrogen peroxide give results which are very accurate. The addition of hydrogen peroxide in no way affected the accuracy of the analysis, but did shorten considerably the time required for the completion of the determination. The time saved by the use of the strong hydrogen peroxide varied from 37 to 84 per cent—the average saving being 68 per cent.

TABLE I.—DETERMINATION OF NITROGEN IN AMINO COMPOUNDS.

| Organic Compounds. | Time in Minutes. Gunning. | Time in Minutes. Plus $H_2O_2$. | Per Cent Nitrogen. Gunning. | Per Cent Nitrogen. Plus $H_2O_2$. | Theoretical. | Time Saved in Per Cent. |
|---|---|---|---|---|---|---|
| Acetanilid | 89 | 56 | 10.26 | 10.21 | 10.37 | 37.1 |
| Acetphenetidin | 119 | 34 | 7.61 | 7.63 | 7.70 | 71.4 |
| *o*-Aminobenzoic Acid | 60 | 30 | 10.15 | 10.16 | 10.21 | 50.0 |
| *m*-Aminobenzoic Acid | 61 | 32 | 10.18 | 10.13 | 10.21 | 47.5 |
| *p*-Aminobenzoic Acid | 60 | 32 | 10.20 | 10.16 | 10.21 | 46.7 |
| alpha-Amino-*n*-butyric Acid | 123 | 34 | 13.57 | 13.54 | 13.58 | 72.4 |
| alpha-Aminocaproic Acid | 254 | 51 | 10.74 | 10.63 | 10.68 | 79.9 |
| alpha-Aminocaprylic Acid | 250 | 48 | 8.63 | 8.78 | 8.79 | 80.8 |
| alpha-Aminoisobutyric Acid | 131 | 37 | 13.59 | 13.58 | 13.58 | 71.8 |
| Benzidine | 300 | 78 | 15.36 | 15.22 | 15.21 | 74.0 |
| *p*-Bromoacetanilid | 140 | 39 | 6.45 | 6.67 | 6.54 | 72.2 |
| 3-Bromo-4-acetylaminotoluene | 210 | 41 | 5.94 | 5.94 | 6.14 | 80.5 |
| *p*-Bromoaniline | 120 | 39 | 8.05 | 8.17 | 8.14 | 67.5 |
| *o*-Chloroacetanilid | 212 | 33 | 8.20 | 8.19 | 8.26 | 84.4 |
| *p*-Chloroacetanilid | 208 | 38 | 8.42 | 8.40 | 8.26 | 81.7 |
| *p*-Chloraniline | 230 | 49 | 10.85 | 11.04 | 10.99 | 78.7 |
| 1,4 - Diaminobutanehydrochloride | 165 | 37 | 17.38 | 17.32 | 17.39 | 77.6 |
| *p* - Dimethylaminobenzaldehyde | 214 | 79 | 9.26 | 9.19 | 9.39 | 63.1 |
| *o*-Tolylurea | 329 | 89 | 18.44 | 18.46 | 18.65 | 72.9 |
| *p*-Tolylurea | 240 | 76 | 18.48 | 18.46 | 18.65 | 68.3 |
| 2,4,6-Tribromoaniline | 60 | 31 | 4.30 | 4.31 | 4.25 | 48.3 |

A series of compounds, containing nitrogen in the nitro form, were investigated next. These compounds were analyzed according to the procedure outlined above. The results are presented in Table II. From the data included in this table, it may be observed that there was considerable reduction in the clearing time, but there was little agreement in the percentages of nitrogen obtained. With these nitro compounds, the digestion was stopped when the liquid had attained a light straw color, and the nitrogen was determined in the usual manner. It was thought that prolonged heating after the straw color was obtained might increase materially the percentage of nitrogen found. In no case where the heating was continued as long as one hour were quantitative results obtained. Quantitative recovery of nitrogen was not only impossible, but check results could not be obtained when two determinations were performed under exactly the same conditions. Many investigators have reported that nitro compound cannot be determined successfully by the unmodified Gunning method.

TABLE II.—DETERMINATION OF NITROGEN IN NITRO COMPOUNDS.

| | Time in Minutes. | | Per Cent Nitrogen. | | |
|---|---|---|---|---|---|
| | Gunning. | Plus $H_2O_2$. | Gunning. | Plus $H_2O_2$. | Theoretical. |
| *o*-Nitrobenzoic Acid | 330 | 55 | 8.19 | 8.23 | 8.38 |
| | 250 | 30 | 7.76 | 7.76 | |
| *m*-Nitrobenzoic Acid | 270 | 40 | 7.97 | 7.75 | 8.38 |
| | 238 | 46 | 8.28 | 8.16 | |
| *p*-Nitrobenzoic Acid | 270 | 50 | 7.82 | 8.13 | 8.38 |
| | 250 | 33 | 7.71 | 7.48 | |
| *o*-Nitrophenol | 220 | 60 | 9.43 | 7.96 | 10.07 |
| | 170 | 62 | 9.17 | 9.06 | |
| *m*-Nitrophenol | 195 | 75 | 8.92 | 9.67 | 10.07 |
| | 160 | 95 | 9.01 | 9.00 | |
| *p*-Nitrophenol | 250 | 52 | 8.09 | 7.81 | 10.07 |
| | 170 | 63 | 8.22 | 8.41 | |
| *o*-Nitrobenzaldehyde | 120 | 42 | 9.21 | 7.20 | 9.27 |
| | 120 | 40 | 8.31 | 7.30 | |
| *m*-Nitrobenzaldehyde | 126 | 30 | 9.32 | 8.99 | 9.27 |
| | 118 | 32 | 8.42 | 9.00 | |
| *p*-Nitrobenzaldehyde | 125 | 30 | 9.33 | 9.08 | 9.27 |
| | 116 | 28 | 9.28 | 9.07 | |
| 1,2,3-Nitrotoluidine | 150 | 50 | 13.29 | 13.75 | 18.41 |
| | 180 | 52 | 14.91 | 14.00 | |
| 1,3,4-Nitrotoluidine | 165 | 48 | 12.79 | 13.02 | 18.41 |
| | 180 | 53 | 12.67 | 13.02 | |
| 1,2,4-Nitrotoluidine | 165 | 48 | 15.44 | 17.00 | 18.41 |
| | 180 | 52 | 17.29 | 17.27 | |
| 1,2,5-Nitrotoluidine | 150 | 52 | 14.56 | 15.67 | 18.41 |
| | 180 | 50 | 18.02 | 15.01 | |
| 1,4,3-Nitrotoluidine | 165 | 49 | 11.61 | 12.87 | 18.41 |
| | 180 | 51 | 12.32 | 14.19 | |
| *o*-Nitrochlorobenzene | 140 | 55 | 4.29 | 3.73 | 8.89 |
| | 140 | 60 | 5.02 | 5.02 | |
| *m*-Nitrochlorobenzene | 150 | 57 | 3.79 | 3.09 | 8.89 |
| | 200 | 55 | 4.50 | 3.53 | |
| *p*-Nitrochlorobenzene | 200 | 51 | 3.73 | 3.36 | 8.89 |
| | 150 | 47 | 3.41 | 2.58 | |

## CONCLUSIONS.

1. The percentage nitrogen in compounds containing the nitrogen in form of the amino group is rapidly and accurately determined by use of strong hydrogen peroxide in the Gunning method.

2. The addition of hydrogen peroxide does not make possible the determination of nitrogen in organic compounds containing the nitro group.

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## STRYCHNINE IV: LETHAL DOSE STUDIES ON CATTLE AND SHEEP.*

JUSTUS C. WARD AND F. E. GARLOUGH.[1]

The earlier papers in this series (1, 2, 3) have presented data on chemical and physiological tests for strychnine, and on masking of strychnine bitterness by certain chemicals. The present discussion deals with the toxicity of strychnine to cattle and sheep.

Literature on the feeding of measured doses of strychnine to domestic animals to determine the lethal doses is very deficient (4). It is because of this fact that the authors are presenting data accumulated under somewhat adverse conditions, since many more animals were involved in their tests than have been reported upon at any one time previously. In these studies 26 cattle and 65 sheep were used.

The obtaining of such a large number of test individuals was made possible through the coöperation of governmental agencies concerned with the administration of the cattle and sheep-buying programs in Idaho and Wyoming during the fall of 1934. The buying program was carried out as a drought relief measure to prevent starvation of a large number of animals on the depleted ranges during the winter. The animals purchased by the Government were graded down to a class that was called "condemned." These "condemned" animals, by the terms of purchase, were to be slaughtered on the owner's property and were to be destroyed. Many of these individuals were organically sound, but were emaciated to the extent that they would not be able to reach a shipping point in condition to be fed back to usable condition. By following the buying crews it was possible for the authors to obtain animals in fairly good condition for their experiments. The tests were always run with the full knowledge and consent of the owner of the "condemned" stock. Normal stock may differ in susceptibility.

Two major observations were made on each animal studied; *first*, the lethal dose; *second*, the rate and manner in which the animal accepted the ground squirrel poison which was the form in which the strychnine was fed. Because of the fact that both cattle and sheep refused the poisoned grain in many cases it was necessary to resort to forced feeding to obtain the lethal dose data needed. Tabulations will show where this forced feeding was used.

The results seem widely variable, so the correlation of dosage trials will prove of value.

Tables I and II indicate that four of eight "condemned" animals died at 15 mg./Kg.; two of three animals at 16 mg./Kg. and all died at doses of 18 mg./Kg. and above. Doses below 12.50 mg./Kg. were only occasionally dangerous, as in the case of a markedly susceptible animal, since only one of nine cows in this dosage range died.

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* Scientific Section, A. PH. A., Portland meeting, 1935.

[1] Control Methods Research Laboratory, Bureau of Biological Survey, Denver, Colorado.

TABLE I.—STRYCHNINE EFFECTS IN "CONDEMNED" CATTLE.

| Dose, Mg./Kg. | Bait. | Method of Application. | Symptoms. | Results. |
|---|---|---|---|---|
| 20.00 | Bran mash | Forced[1] | Spasms—25 min. | Death—40 min. |
| 18.00 | Grain | Fed | " —42 " | " —90 " |
| 17.80 | Bran mash | Forced | " —15 " | " —20 " |
| 17.50 | Grain | Fed | Completely refused the bait | — Shot |
| 17.50 | " | " | " " " " | " |
| 16.00 | Bran mash | Forced | Spasms— 2 hours | Death— 4 hours |
| 16.00 | " " | " | " —33 min. | " —43 min. |
| 16.00 | " " | " | Stiff—no spasms | Survived 4 1/2 hours; shot |
| 15.00 | " " | " | Spasms—30 min. | Death—60 min. |
| 15.00 | Grain | Fed | None | Survived 4 hours; shot |
| 15.00 | " | " | Slightly nervous | " 2 " " |
| 15.00 | Bran mash | Forced | None | " 9 " " |
| 15.00 | " " | " [2] | Spasms—8 min. | Death—10 min. |
| 15.00 | " " | " | " —40 " | " —95 " |
| 15.00 | " " | " | " —35 " | " —80 " |
| 15.00 | " " | " | Slightly nervous | Survived |
| 12.50 | Grain | Fed | " " | Survived 4 hours; shot |
| 12.50 | " | " | None | Survived 2 1/2 hours; shot |
| 12.00 | Bran mash | Forced | " | Survived 6 1/2 hours; shot |
| 12.00 | " " | " | Slight spasm 2 1/2 hours | Survived 6 1/4 hours; shot |
| 12.00 | " " | " | None | |
| | After 18 hours animal normal | | Force fed 15 mg./Kg. more | Survived both doses |
| 10.00 | Grain | Fed | Spasms—32 min. | Death—60 min. |
| 10.00 | " | " | None | Survived 3 hours; shot |
| 10.00 | Bran mash | Forced | None | Survived 3 hours; shot |
| 8.00 | " " | " | " | Survived 2 1/2 hours; shot |
| 5.00 | " " | " | " | Survived 3 hours; shot |

[1] These animals refused to eat the poisoned grain offered, so they were force fed the bran mash.

[2] This animal was highly nervous and excitable.

TABLE II.—CORRELATION OF STRYCHNINE EFFECTS IN "CONDEMNED" CATTLE.

| Dose, Mg./Kg. | Results. | |
|---|---|---|
| 20.00 | One animal fed this dose died in 40 min. | 1/1 (40 min.) |
| 18.00 | " " " " " " " 90 " | 1/1 (90 ") |
| 17.80 | " " " " " " " 20 " | 1/1 (20 ") |
| 17.50 | Two animals " " " refused to eat | 0/2 (—, —) |
| 16.00 | Two of three animals fed this dose died in 42 min. and 4 hours, respectively. One survived | 2/3 (42 min., 4 hours) |
| 15.00 | Four of eight fed died in 60, 10, 95 and 80 min. | 1/2 (60, 10, 96, 80 min.) |
| 12.50 | Two of two animals survived | 0/2 (—, —) |
| 12.00 | " " " " | 0/2 (—, —) |
| 10.00 | One of three died in 60 min. | 1/3 (60, —, —) |
| 8.00 | One animal survived | |
| 5.00 | " " " | |

To determine what these figures would mean in terms of a ground squirrel poison containing 1 ounce of strychnine to each 10 quarts of steam-rolled oats—the strongest formula generally used in the areas where these animals were tested—the following computations are made. Assuming 15 mg./Kg. as a possible killing dose ($LD_{50\%}$), 1/10 of a grain of strychnine per pound of cow would be needed. This means 1.23 Gm. or 80 grains, for the average 800-pound "condemned" adult cow.

In the "1 to 10" ground squirrel poison, these 80 grains would be carried on 1 pound 15 ounces of the steam-rolled bait. Recalling how difficult it was to find even a "condemned" animal that would eat half this quantity of such bait, one can safely conclude that properly distributed ground squirrel poison carries no hazard to cattle. Furthermore, in heavy ground squirrel infestation this 1 pound 15 ounces of poison would be distributed over approximately 4 acres of cattle range. To obtain a possible killing dose, it would, therefore, be necessary for the "condemned" cow to eat every bait on the entire 4 acres, which is inconceivable.

Correlations of data following normal feeding of sheep (Table III) are somewhat badly spotted owing to very slow acceptance of the poison and to the necessity of killing the animals after a maximum of three hours in order that the skinning crew could maintain its schedule. This series does not indicate, however, that 12.50 mg./Kg. would be the dangerous dose for the average animal.

TABLE III.—STRYCHNINE EFFECTS IN "CONDEMNED" SHEEP.

(*a*) Normal feeding—salt baited—but not forced.

| Dose, Mg./Kg. | Method of Application. | Symptoms. | Results. |
|---|---|---|---|
| 25.00 | Fed | Spasms—89 min. | Death 2 hours |
| 24.20 | " | Nervous—3 hours | Killed for crew 3 hours |
| 24.30 | " | Spasms—61 min. | Death 96 min. |
| 18.40 | " | Spasms—86 " | Death 96 " |
| 17.10 | " | Nervous—3 hours | Killed for crew 3 hours |
| 14.70 | " | Spasms—84 min. (up) | " " " 3 " |
| 12.50 | " | Spasms | Death 60 min. |
| 12.50 | " | None | Killed for crew 3 hours |
| 10.10 and 10.00 | " | " | " " " 3 " |
| 6.80 and 6.80 | " | " | " " " 3 " |
| 6.40 | " | Spasms—32 min. | Death 58 min. |
| 5.00 and 4.10 | " | None | Killed for crew 3 hours |

(*b*) Forced feeding.

| Dose. | No. Animals per Dose. | Symptoms. | Results. |
|---|---|---|---|
| 40.00 | 2 | Spasms 34, 13 min. | Death 52, 18 min. |
| 35.00 | 1 | " 25 " | " 44 |
| 30.00 | 2 | " 17, 11 " | " 27, 19 |
| 28.00 | 1 | " 17 | " 25 |
| 27.50 | 2 | " 25, 170 | " 40, 200 |
| 25.00 | 3 | " 15, 21, 54 | " 26, 30, 74 |
| 22.50 | 2 | " 33, 30 | " 41, 35 |
| 20.00 | 3 | " 49, 21, —. | " 56, 53, over night |
| 17.50 | 3 | " 33, —, — | " 58, ON, killed |
| 15.00 | 3 | " 81, 105, — | " 109, 110, " |
| 12.50 | 10 | " 64, 36, 76, —, —. —, —, —, —, —, | " 74, 57, 129, 6 hours ON, ON, ON, ON, —, —. |
| 10.00 | 10 | " 2½ hours —, —, —, —, —, —, —, —, —, | ON, ON, ON, ON, ON, —, —, —, —, —. |
| 7.50 | 2 | None | Survived |

Forced feeding data indicate that 10 mg./Kg. ($^1/_{14}$ grain per pound) would be a dangerous dose for "condemned" sheep. Approximately 6 grains (360 mg.) of

strychnine might kill an 80-pound sheep. From these figures it appears that slightly more than 3 ounces of a 1 to 10 formula might kill a sheep. These 3 ounces of poisoned grain would be exposed on approximately 1 acre of ground squirrel-infested sheep range. It is inconceivable that a sheep might get all the poisoned grain from an acre, even if feed on the pasturage was extremely short.

To test whether or not the amount of strychnine in the mixture would alter the animals' acceptance, a 1 to 16 bait prepared with a large amount of free salt in it was offered to six additional "condemned" sheep. They were allowed to eat all they would, then the balance was weighed back and the dose taken was computed.

ACCEPTANCE TEST 1 TO 16 POISONED GRAIN-FED SHEEP.

| Dose Eaten, Mg./Kg. | 1 to 16 Bait, Ounces. | Result. |
|---|---|---|
| 4.85 | 2 | No symptoms in 3 hours. |
| 7.00 | 2 3/4 | No symptoms in 3 hours |
| 6.70 | 2 3/4 | Very nervous. Killed after 1 1/4 hours |
| 10.95 | 4 1/2 | Slightly nervous. Killed after 1 1/4 hours |
| 12.40 | 6 1/4 | Stiff. Killed over night |
| 18.50 | 7 3/4 | Spasm 68 min. Dead 85 min. |

From this record it would appear that where the grain is available in a formula carrying a high percentage of salt there is a higher palatability factor. For that reason care should be exercised with somewhat greater diligence when salty formulas are used on sheep ranges, particularly during these periods of the year when the grass is short and the animals are cropping very closely.

## CONCLUSIONS.

1. Strychnine in the form of a 1 to 10 ground squirrel poison is not readily taken by either cattle or sheep.

2. There would be needed 1 pound 15 ounces of this 1 to 10 formula to carry a lethal dose for an 800-pound "condemned" cow, and slightly more than 3 ounces for an 80-pound "condemned" sheep.

3. The susceptibility of normal (healthy) animals might differ from that of "condemned" animals.

4. Because of the slowness with which these animals accepted ground squirrel poison voluntarily, many of the tests reported were based on force-feeding methods. This system of administration excited the animals and tended to lower the lethal dose.

5. Because of the small bait spots used in ground squirrel control operations, to get a possible killing dose, a cow would have to pick up *all* the scattered grain from about 4 acres, and a sheep from 1 acre of range.

6. Properly exposed ground squirrel poison offers no hazard to cattle and only a slight hazard to sheep.

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# EPHEDRINE SYNTHESIS I: THE PREPARATION OF PROPIOPHENONE DIETHYL ACETAL AND OF 1-PHENYL-1-ETHOXY-PROPENE-1.[1]

BY ERNEST L. BEALS WITH F. A. GILFILLAN.[2]

Ephedrine, the chief alkaloid in the Chinese drug Ma Huang, was discovered by Nagai (1) in 1887. Its constitution was shown by Späth and Göhring (2) to be represented by the formula: $C_6H_5{\cdot}CHOH{\cdot}CH(NHCH_3){\cdot}CH_3$. Since this contains two asymmetric carbon atoms, four optically active forms may exist, together with racemic or other mixtures of these four. The two active forms in which the hydroxyl and methylamino groups are adjacent were believed to represent *l*- and *d*-ephedrine: the two in which these groups are on opposite sides of the axis, to represent *l*- and *d*-pseudoephedrine (3).

Both ephedrine and pseudoephedrine have been synthesized by various procedures, but the exact relationship existing between them seems still a matter of some doubt (4). The present investigation is an attempt to throw additional light upon this question.

## EXPERIMENTAL.

*Propiophenone Diethyl Acetal.*—The method employed follows that of Claisen (5) in which one mole of ketone in 3 moles of alcohol is treated with 1.1 mole of ethyl orthoformate in the presence of a catalyst (6, 7). Into an Ehrlenmeyer flask were put 72 Gm. of propiophenone, 88 Gm. of ethyl orthoformate, 84 Gm. of absolute alcohol and 0.3 cc. of 36% hydrochloric acid. The temperature increased about ten degrees, and after several hours there developed a beautiful cerise color which gradually faded into yellow. At the end of 24 hours the product was neutralized with alcoholic KOH and the ethyl formate, alcohol and excess orthoformic ester were removed by distillation. The acetal was fractionated under reduced pressure with yields, in successive operations, of 97.9%, 96.2%, 96.5% and 97.6% of the theoretical.

The product was a colorless, mobile liquid with a faint aromatic odor. A cryoscopic determination of the molecular weight in benzene showed 207.45. (Calculated for $C_6H_5{\cdot}C(OC_2H_5)_2{\cdot}C_2H_5$ was 208.2.) Its boiling point under varying pressure was: (6 mm. = 93–96°), (8 mm. = 99–100°), (10 mm. = 100–101°), (14 mm. = 108–110°), (23 mm. = 119°) and (760 mm. = 226–228°). When boiled at atmospheric pressure, there was a slight decomposition into the monoethyl derivative. The refractive index was $d_{25} = 1.4767$. The specific gravity 25°/4° was 0.94476.

*1-Phenyl-1-Ethoxy-Propene-1.*—When propiophenone diethyl acetal was boiled for some time under atmospheric pressure, it was partially decomposed into the monoethyl derivative and ethyl alcohol. In order to carry this decomposition to completion, some agent must be introduced as an alcohol acceptor (8). Acetyl chloride serves very well in this capacity, but since one by-product resulting is hydrochloric acid, which would effect complete hydrolysis of the acetal, this must be neutralized as formed. Pyridine functions admirably for this purpose.

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[1] Reconstructed from a thesis by Ernest L. Beals presented in partial fulfilment of the requirements for the degree of Master of Science at the Oregon State College.

[2] Professor of Pharmacy, Oregon State College.

To a mixture of 25 Gm. of propiophenone diethyl acetal with 10 Gm. of pyridine, 10 Gm. of acetyl chloride was slowly added with stirring, the mixture being chilled with ice and salt. The odor of pyridine disappeared, the contents of the flask becoming a pasty white mass. After standing fifteen minutes, a slight excess of pyridine was added, and the reaction was allowed to stand over night. Ether was then added and the flask contents were filtered, washing the precipitated pyridine hydrochloride with ether. The filtrate was distilled, removing in order the ether, ethyl acetate and pyridine. The liquid remaining in the flask was distilled under reduced pressure, practically all passing over at 105° under 19 mm. pressure. The yields on two successive runs were 83.6% and 92.8% of the theoretical.

The product was a colorless aromatic liquid, immiscible with water, and readily hydrolyzed by acids, yielding the original ketone. It developed a pale yellow color when boiled for some time at atmospheric pressure. It instantly decolorized a solution of bromine in carbon tetrachloride. A determination of its molecular weight by the freezing-point method in benzene gave a value of 161. (Calculated for $C_6H_5{\cdot}C(O{\cdot}C_2H_5){:}CH{\cdot}CH_3$ was 162.) The boiling point under varying pressure was: (12 mm. = 95–96°), (16 mm. = 100–101°), (19 mm. = 105°) and (760 mm. = 220–221° corr.). At 25° the refractive index lay between 1.5207 and 1.5210, and the specific gravity at 25°/4° was 0.95441.

In attempting to convert this compound into racemic ephedrine, some difficulties were encountered which have not as yet been overcome, but the investigation is to be continued.

## SUMMARY.

1. In attempting to synthesize ephedrine by a new method, a new compound was produced, propiophenone diethyl acetal, the physical constants of which were determined.

2. This acetal was converted into an unsaturated compound, also new in the literature, 1-phenyl-1-ethoxy-propene-1, the physical constants of which were also ascertained.

3. Work will be continued on converting this unsaturated compound into ephedrine.

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## SCHEELE SESQUICENTENNIAL.

German apothecaries held a Scheele memorial meeting in coöperation with the Society for the History of Pharmacy, in Stralsund, May 17th. Carl Wilhelm Scheele was born in Stralsund, December 1742; he died in Köping, May 1786. Swedish apothecaries participated in the memorial meeting; the addresses of the occasion included one on Scheele—the man, and another as the scientist. Scheele was employed for a number of years in the Apotek which he acquired in 1776, and here he died ten years later. Observation, experimentation and sacrificing devotion gained for him surpassing eminence.

# CORRECTABLE PHARMACEUTICAL AND CHEMICAL INCOMPATIBILITIES.*

BY GEORGE L. SECORD.

The problem which gives the prescription pharmacist the greatest concern and the subject which enters into all branches of pharmaceutical learning, is *Incompatibility* involving more particularly the pharmaceutical and chemical types. The degree of permissible deviation from the prescription proper, is a matter of considerable controversy with many pharmacists, due largely to an inferiority complex, a lack of sufficient therapeutic knowledge or an unwarranted fear that any modification of the prescription would either change it medicinally or that such a change would meet with disfavor on the part of the physician.

No calling of any consequence was ever practiced by "rule of thumb." Both pharmacy and medicine are extremely broad in their application, and just as the physician's selections of remedies must be varied with the patient's needs, so the pharmacist must adjust his training to the peculiarities of the prescription.

Obviously, no agent should be used which increases the danger, changes the appearance, permanency, uniformity of dose or intended effectiveness which would in any manner, or in any material degree, alter the medicinal effect from that originally intended by the physician. *Correctives* then, in this sense, should be employed in the minimum quantities and only those *Changes* resorted to under this order of things which would be important therapeutically and acceptable to the physician, realizing that in every case the finished product must represent the original intent of the physician in its fullest measure. This thought is always an element of the greatest importance.

It is a matter of record that opinions of pharmacists are sought more and more by the members of the medical profession. Experience teaches them to respect the training and ability of the men who carry on the ethical practices of our profession. Confidence and recognition for the pharmaceutical profession must be established, if pharmacists are to fulfil in the greatest measure the type of service that is expected of them—in the face of certain interests that have unfortunately swept the country, and who by their persistency have crushed out a large part of pharmacy's rightful practice and flooded the country with high-priced specialties. Notwithstanding this vigorous campaign, the courage of pharmacists is demonstrated by progress and the study of incompatibilities presents a phase of pharmaceutical and medical research.

It is of fundamental importance that pharmacists strive for professional recognition and advancement.

The incompatibilities presented are studies of some of the more common problems which frequently confront the pharmacist. It is not intended that these prescriptions with the accompanying remarks convey anything particularly unusual to the prescription pharmacist, but they have proved satisfactory over a long period of years.

PHARMACEUTICAL AND CHEMICAL INCOMPATIBILITIES.

| | | |
|---|---|---|
| ℞ 1 | Acetylsalicylic Acid | 10 |
| | Potassium Citrate | 10 |
| | Syrup, Water *q. s.* } of each | 60 |

* Section on Practical Pharmacy and Dispensing, A. PH. A., Portland meeting, 1935.

This is a typical example of the every-day prescription in a drug store when for the purpose of convenience the physician desires to present the medication in liquid form.

Acetyl Salicylic Acid being only partially soluble in this proportion, even in the presence of the potassium citrate, which contributes to its solubility, separates from the main body of the liquid and is partially deposited and suspended on the surface. The rapidity with which this separation takes place does not permit of a uniform dose even when the mixture is thoroughly shaken and, therefore, it becomes necessary to add an agent of suspension for the purpose of increasing the viscosity and thereby preventing the easy separation of this insoluble material. The substance best adapted to this prescription is tragacanth; 5 grains will accomplish the object desired, holding the insoluble Acetyl Salicylic Acid in a highly uniform degree of suspension until a dose can be poured.

| | | |
|---|---|---|
| ℞ 2 | Fluidextract of Iris | 5 |
| | Aromatic Elixir *q. s.* | 60 |

This prescription clearly demonstrates a type of pharmaceutical incompatibility resulting from a change in menstrua. The resinous character of iris requires approximately 80% of alcohol. This is also true for drugs like buchu. When galenical preparations of this kind are brought in contact with vehicles such as Elixir of Pepsin Compound and Aromatic Elixir which are relatively low in alcoholic content a lowering of alcoholic percentage takes place with resulting precipitation. The correction is by addition of sufficient alcohol to prevent this precipitation. When two or more galenicals are present, one with a high alcohol content and another with a relatively low content, obviously, there cannot result a thoroughly clear liquid since an intermediate alcohol content must prevail, that is, an average between that of each of the preparations present. The correction was made with 4 drachms of alcohol.

| | | |
|---|---|---|
| ℞ 3 | Bismuth Subnitrate | 8 |
| | Phenyl Salicylate | 4 |
| | Syrup, Water } of each *q. s.* | 60 |

This prescription carries two insoluble substances—bismuth subnitrate and phenyl salicylate. While bismuth subnitrate is an impalpable powder, phenyl salicylate is a crystalline body requiring careful treatment in a mixture of this kind. The *modus operandi* is to reduce the phenyl salicylate to a fine powder in a mortar and mix thoroughly with the bismuth subnitrate. To this the syrup is added gradually and finally the water. Heat should never be employed in a preparation of this kind, since it fuses the phenyl salicylate and permits it to recrystallize in the mixture.

Both bismuth subnitrate and phenyl salicylate separate rapidly from this mixture and as a consequence must receive proper attention. The correction is made with 5 grains of tragacanth which is mixed intimately with the powders before the addition of the Syrup. Its presence increases the viscosity of the preparation preventing the ready separation of the insoluble bodies.

| | | |
|---|---|---|
| ℞ 4 | Citrated Caffeine | 0.03 |
| | Acetyl Salicylic Acid | 4.0 |
| | Phenacetine | 2.0 |
| | Elixir Pepsin Compound *q. s.* | 60.0 |

This prescription presents another type requiring a suspension agent. Here again tragacanth is the preferred substance; however, owing to the alcoholic content of the Elixir of Pepsin Compound, 7 grains of tragacanth are required to accomplish the object desired.

| | | |
|---|---|---|
| ℞ 5 | Adrenalin Chloride Sol. | 4.0 |
| | Menthol, Camphor } of each | 0.03 |
| | Olive Oil *q. s.* | 30.0 |

Owing to the aqueous nature of solution of adrenalin chloride, it is immiscible with the menthol, camphor, olive oil. Correction is made by obtaining permission from the physician to use the practical equivalent in an oil solution, namely, adrenalin inhalant, ℞ 6. The same prin-

ciple is portrayed in prescription 6, wherein through ignorance of solubility the physician has prescribed ephedrine sulphate in place of ephedrine alkaloid.

| | | | |
|---|---|---|---|
| ℞ 6 | Ephedrine Sulphate | | 0.30 |
| | Menthol<br>Camphor } of each | | 0.015 |
| | Olive Oil<br>Liquid Petrolatum } of each *q. s.* | | 30.0 |

The correction is in obtaining the permission of the physician to substitute ephedrine alkaloid in an equal amount for the ephedrine sulphate thus providing for a relatively clear preparation.

| | | |
|---|---|---|
| ℞ 7 | Spirit Nitrous Ether | 15.0 |
| | Potassium Citrate | 30.0 |
| | Water *q. s.* | 60.0 |

Potassium citrate is very soluble in water and nearly insoluble in alcohol. When a nearly saturated solution in water is prepared, as in this instance, this solution becomes immiscible with the Spirit of Nitrous Ether, which is alcoholic, and the two substances are noticeably separated and mix with difficulty. The speed with which the separation takes place prevents the giving of a uniform dose. The correction is in the dilution of the prescription to twice its quantity with water and doubling the dose. Potassium citrate is not thrown out of solution for the reason that the affinity of the water for this substance is greater than for the alcohol.

| | | |
|---|---|---|
| ℞ 8 | Solution Aluminum Acetate | 12 |
| | Hydrous Wool Fat | 5 |
| | Petrolatum *q. s.* | 30 |

In the foregoing an ointment is wanted and the physician expects, owing to the properties claimed for wool fat, that the 12 cc. of solution of aluminum acetate will be picked up with the 5 Gm. of wool fat. This is erroneous since the hydrous wool fat will not take care of that quantity of fluid. The correction is in substituting 5 Gm. of Aquafor for an equal weight of petrolatum.

| | | |
|---|---|---|
| ℞ 9 | Zinc Sulphate | 0.03 |
| | Water | 2.0 |
| | Sol. Adrenalin Chloride | 3.0 |
| | Petrolatum, white | |

This prescription is intended for an eye ointment. The 3 mg. of zinc sulphate are dissolved in water, solution of adrenal in chloride added and this added to 25 Gm. of white petrolatum. The ointment as prepared would appear to be free from criticism, but upon standing a short time separates water, due to the immiscibility of this quantity of aqueous material with Petrolatum. The correction is in substituting 5 Gm. of Aquafor for an equal weight of white petrolatum.

| | | |
|---|---|---|
| ℞ 10 | Fluidextract Buchu | 10 |
| | Aromatic Elixir | 50 |

Opportunity is taken to show the application of the Elixir Iso-Alcoholic advocated by Dr. Bernard Fantus, of the University of Illinois College of Medicine. Fluidextract of Buchu is shown with aromatic elixir resulting in the profuse separation of the resinous constituents of the drug.

Buchu is also shown with Elixir Iso-Alcoholic which results in a beautifully clear liquid. Elixir Iso-Alcoholic means of the same strength. In other words Fluidextract of Buchu has an alcoholic strength of 80%. To be essentially miscible with it, Elixir Iso-Alcoholic should be of the same strength. In making this Elixir an elixir of low alcoholic content is employed, 5%, and a high one of 90%. These two preparations are used in various proportions to obtain an alcoholic preparation of the desired strength.

| | | |
|---|---|---|
| ℞ 11 | Spirit Nitrous Ether | 8.0 |
| | Potassium Iodide | 2.5 |
| | Syrup | |
| | Water *q. s.* | 30.0 |

Most specimens of Spirit of Nitrous Ether present an acid reaction due either to errors in manufacture or the breaking down of ethyl nitrite through long standing. It is a well-known fact that nitrous acid is incompatible with iodides, and since Spirit of Nitrous Ether is a solution of ethyl nitrite, a reaction naturally follows with liberation of iodine turning the prescription a bright red.

The correction is in neutralizing the free acid in the spirit of nitrous ether before adding it to the other ingredients, preferably with some agent like potassium bicarbonate. Prescriptions thus prepared have kept for several years without liberation of iodine.

| | | |
|---|---|---|
| ℞ 12 | Potassium Iodide | 5.0 |
| | Sodium Nitrite | 2.0 |
| | Syrup of Squill | 15.0 |
| | Water *q. s.* | 120.0 |

This prescription presents the same type of incompatibility as No. 11 in a little different way. Sodium nitrite is used in the presence of potassium iodide and syrup of squill which is acid. Acetic acid breaks down the sodium nitrite forming nitrous acid which is incompatible with potassium iodide, liberating free iodine.

The correction is in obtaining the physician's permission to use an equivalent amount of another preparation of squill which is free from acid, preferably an equivalent amount therapeutically of the fluidextract which is free from acid.

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|---|---|---|
| ℞ 13 | Compound Solution Iodine | 10 |
| | Elixir Iron Quinine and Strychnine N. F. *q. s.* | 120 |

This prescription presents another chemical incompatibility resulting in the precipitation of the alkaloids of quinine and strychnine.

The correction is in raising the alcoholic content of the preparation to a point where the quantities of these substances present will be soluble. This is accomplished with 8 cc. of alcohol substituted for an equivalent amount of the Elixir of Iron Quinine and Strychnine before the addition of the Lugol's Solution.

| | | |
|---|---|---|
| ℞ 14 | Codeine Sulphate | 0.6 |
| | Potassium Bromide | 40.0 |
| | Syrup | |
| | Water of each *q. s.* | 120.0 |

The codeine previously dissolved in a part of the water is added to a solution of potassium bromide in the balance of syrup and water with the almost immediate formation of a white precipitation of codeine alkaloid. The corrective measure is to replace 10 cc. of the water with alcohol and add the solution of codeine sulphate to this mixture. The alcohol acts dissolving upon the codeine alkaloid and prevents its precipitation. A prescription of this kind as corrected is acceptable to the physician and safe for use by the patient.

| | | |
|---|---|---|
| ℞ 15 | Strychnine Sulphate | 0.020 |
| | Potassium Iodide | 5.0 |
| | Syrup | 15.0 |
| | Water *q. s.* | 120.0 |

To strengthen the reaction 10 times this quantity of strychnine was used.

This presents the same problem as given in the preceding prescription, but owing to the small dose of strychnine, it is somewhat more treacherous. Strychnine is deposited as a white crystal and as such is difficult to detect. The corrective measure is as before, namely, alcohol in sufficient amount, approximately 6 cc., which acts dissolvingly upon the alkaloid keeping it safely in solution. For purposes of exhibit the quantity of strychnine is increased 10 times.

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| ℞ 16 | Tincture Digitalis | 10.0 |
| | Morphine Sulphate | 0.5 |
| | Liquor Potassium Arsenite | 12.0 |
| | Peppermint Water *q. s.* | 120.0 |

The incompatibles are morphine sulphate and the potassium arsenite solution which is decidedly alkaline. Since there is insufficient alcohol present to keep the precipitated morphine in solution, more alcohol must be added; 12 cc. are necessary.

| | | |
|---|---|---|
| ℞ 17 | Soluble Ferric Phosphate | 12.0 |
| | Acid Phosphoric | 8.0 |
| | Strychnine Sulphate | 0.030 |
| | Elix Aromatic | |
| | Cinnamon Water of each *q. s.* | 120.0 |

Sodium citrate in ferric phosphate is the substance which makes ferric phosphate soluble. In the presence of phosphoric acid, the sodium citrate is converted into sodium phosphate resulting in the precipitation of ferric phosphate. To prevent the precipitation it is necessary to add 3 drachms of sodium citrate to the three drachms of ferric phosphate solution, or use 10% solution of meta-phosphoric acid in a mortar and dissolve—add the remainder of water and finally the phosphoric acid—a clear solution results.

| | | |
|---|---|---|
| ℞ 18 | Betanaphthol | 0.60 |
| | Balsam Peru | 8.0 |
| | Acid Salicylic | 2.0 |
| | Olive Oil | 45.0 |
| | Lime Water *q. s.* | 120.0 |

Since both an acid and alkali are present some trouble should be expected. When the lime water is added to the olive oil a small amount of calcium oleate is formed which in turn emulsifies the balance of the olive oil. To this mixture, the betanaphthol dissolved in a small amount of alcohol is added, then the Balsam of Peru, warmed and added very gradually under shaking or mixing in a mortar and, lastly, the salicylic acid also dissolved in a small amount of alcohol. As soon as the salicylic acid is added, calcium salicylate is formed which releases the calcium from the calcium oleate thus destroying the insoluble soap, which in turn removes the agent of emulsification, and the preparation becomes an unsightly mixture.

To correct, it is necessary to consult the physician and obtain his permission to eliminate either the salicylic acid or the lime water. If the lime water is eliminated an ordinary emulsion with acacia can be easily prepared resulting in the same type of mixture. The Balsam of Peru is somewhat troublesome, but can be properly handled through careful emulsification in the mixture.

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| ℞ 19 | Crude Coal Tar | 6.0 |
| | Solution Aluminum Subacetate | 12.0 |
| | Petrolatum *q. s.* | 60.0 |

Crude coal tar and solution of aluminum subacetate are not throughly picked up by the petrolatum. The crude coal tar remains stringy and the solution of aluminum subacetate separates in drops.

To correct, it is necessary to substitute 10 drachms of Aquafor for an equal amount of petrolatum when a smooth and homogeneous ointment is produced.

| | | |
|---|---|---|
| ℞ 20 | Mercurochrome | 1 |
| | Water | 10 |
| | Petrolatum | 20 |

The physician has intended the petrolatum to pick up the water, necessary for solution of Mercurochrome. This, however is not accomplished. The pharmacist has one of two suggestions to offer to the physician:

1. To substitute a part (10 Gm.) of the petrolatum with wool fat.
2. To substitute 5 Gm. of petrolatum with an equal weight of Aquafor.

Owing to the simplicity of handling, the latter method is shown here in the exhibit—(at the meeting).

# PHARMACY IN MISSISSIPPI.*

BY LEW WALLACE.[1]

It has been a pleasure to look back through the years and study the thoughts of the men who have helped to shape the destiny of our profession in this state since the earliest days. The idea of making the practice of pharmacy a privilege under the law was conceived, and to this end the first meeting of the Mississippi State Pharmaceutical Association was held in the Senate chamber at the capital, June 12, 1883.

A number of pharmacists from all sections of the state met in response to the following call:

"*Mississippi State Pharmaceutical Association.*—The time seeming propitious and the state of our profession demanding it, we, the undersigned druggists of the state of Mississippi, deem it proper to call for a convention to be held at Jackson, June 12, 1883, for the purpose of organizing a State Pharmaceutical Association. The object of the association will be to unite its members in the bonds of fellowship and common interest, that they may coöperate in elevating the profession, as well as protecting it from the many evils which now affect our trade. We sincerely trust that this effort will receive the hearty and generous support of every druggist in the state, feeling assured that it will prove a great benefit to all. The time and place designated for this convention was selected in view of the fact that June is usually a dull month in trade, and Jackson is the most central, as well as the most accessible point in the state." This meeting was attended by about 30 pharmacists.

These men, feeling that organization, unity of action and comparison of ideas were essential to the advancement of any cause, and believing that there was room for the elevation and extension of pharmaceutical knowledge among the druggists of the state, that there existed a necessity for some supervision of the dispensing of drugs and medicine, both for their own and the general welfare, and that such results could best be accomplished by a State Pharmaceutical Association, passed a resolution as follows:

*Resolved*, That we, druggists and apothecaries from different parts of the state, who are now assembled in convention in the city of Jackson, do hereby organize ourselves into a permanent association for the purpose of accomplishing such results, and that we adopt a constitution and by-laws.

Thereupon, according to the record, a constitution and by-laws was adopted. To this day the wisdom and forethought of those men are very much in evidence in the present constitution and by-laws of the Mississippi State Pharmaceutical Association.

We find that the pioneers in pharmacy of this state in the initial meeting of our Association expressed themselves as having for their aim the uniting of the reputable pharmacists of Mississippi for mutual protection, assistance, encouragement and improvement. To encourage scientific research, to develop pharmaceutical talent, to elevate the standards of our professional thought and, ultimately, to restrict the practice of pharmacy to properly qualified druggists and apothecaries.

Our first pharmacy legislation was enacted into law in 1892, and some time later an additional law was enacted, creating the Board of Pharmaceutical Examiners. In 1921 our law requiring college graduation from a recognized college of

* Section on Education and Legislation, A. PH. A., Portland meeting, 1935.

[1] Laurel, Miss.

pharmacy was made a part of the Mississippi Code, and since that day, pharmacy has looked upward and to better things in Mississippi.

The passage of the prerequisite requirements was not an act of chance, and a résumé of the advancement of pharmacy in Mississippi would be sadly lacking, if it failed to touch even sparingly the life and work of at least a few of the noble men who have stood by our profession through the years.

Early after the beginning of the twentieth century, a young man with a vision fought long and hard for pharmacy, and about 1908, succeeded in having established at the University of Mississippi a department of pharmacy. This man, who was none other than our present well-loved Henry Minor Faser, was unanimously elected dean of the School of Pharmacy and was the first to open its doors to the youth of Mississippi. The School of Pharmacy was housed in a small part of the basement of one of the oldest buildings at Oxford. But in the few short years between 1908 and 1921, the energetic leadership of Dr. Faser, as he is affectionately known to hundreds of Mississippi pharmacists, carried his department from its humble beginning in the basement of an old building to an outstanding place among the façades of the campus. Due to Dr. Faser's untiring efforts, there was erected in a prominent part of the campus circle a $350,000.00 pharmacy building, with all modern equipment and conveniences. It was a sad day for Mississippi pharmacy when Dr. Faser, some eight years ago, resigned as dean of the School of Pharmacy. But through every dark cloud there is a silver lining, and we found our ray of hope that his place could be filled when the State of Mississippi secured as the dean of our School of Pharmacy, Elmer L. Hammond, a man in whom we are justly proud and a man who has adequately and fittingly upheld the traditions of the School of Pharmacy at "Ole Miss." Dean Hammond has won a place in the hearts of Mississippi pharmacists and has had a very important part in shaping our activities.

The Legislative Committee added very little to our pharmacy laws from 1921 to 1934. However, the members of our Association were active during these years and did many things to improve conditions. Outstanding during this time was the proposal of President Charles E. Wilson, of the Association, about four or five years ago, when his plan of a paid business manager was adopted at Vicksburg and unanimously supported by the druggists of Mississippi. Claude E. Anding of Flora, Mississippi, was elected as our first paid business manager. Mr. Anding did wonderful work throughout Mississippi for the cause. But after a time the program was discontinued because it was found impossible to put through our measure due to the fact that our efforts were directed against issues controllable only by legal procedure, and Mr. Anding and the members of our official family had nothing more than the backing of a voluntary organization. Such men as S. B. Key, present secretary of the Mississippi Pharmaceutical Association, Fred W. Duckworth, prominent and valuable member of our organization, H. B. McInnis, Lumberton; Chester F. Jones, Jackson; G. W. Harrison, Forest; P. K. Thomas, Tupelo; B. W. Johnson and J. L. Hicks, Laurel, Mississippi; W. J. Cox, Batesville; Sam McDuffey, Nettleton, and Charles E. Wilson, director of our U. S. P. and N. F. Program, along with many others, were outstanding during these years for the betterment of conditions in Mississippi pharmacy. To their untiring efforts and suggestions is due the credit for the launching of our present program that is backed by the mandate of organized society and has for its objective the creation of a strong

and determined desire in the minds of the pharmacists in this state to stand by their profession in order that the public will stand by them.

On March 9, 1934, there was enacted into law that part of chapter 338 of the Mississippi Code known as House Bill No. 155. This legislation, designed to throw a protective band around the profession of pharmacy, includes everything in the way of drugs and medicine other than patent, proprietary and household remedies. Our Legislative Committee, guided by the experience of pharmacists in other states and ably assisted by T. O. Slaughter, Waynesboro, saw fit to exempt these medicines, feeling that there was little need for legislation to cover their sale and distribution. The Legislative Committee, with reference to this controversial subject, felt that regulation should begin with the manufacture and end with the pharmacist.

Pharmacy in Mississippi to-day has more than one leg upon which to stand, and we are at this time engaged in the multiple task of strengthening these legs to put our profession in the high position it deserves. We are advocating—and there is every indication that we shall carry to a successful conclusion—the formation of what we are pleased to call a Southeastern Drug Club composed of several southern states to band together for mutual protection. At the convention of last June we adopted a program of U. S. P. and N. F. extension similar to other U. S. P. and N. F. plans, and Charles E. Wilson, Corinth, Mississippi, was unanimously elected as the Director of this division of our program. We have an active paid committee whose duty it is to seek ways and means of coöperating with each division of organized activity within this state for the purpose of exchanging suggestions and to establish a spirit of coöperation.

We are face to face with our problems and realize that we have a tremendous task in front of us, but when we think back over the record of the AMERICAN PHARMACEUTICAL ASSOCIATION and other organizations that have so long championed the cause of pharmacy, we are encouraged by a knowledge of their achievements and are determined to carry on.

The pharmacists of Mississippi are proud of their national organization, the AMERICAN PHARMACEUTICAL ASSOCIATION, and have a deep and sincere interest in the success of its undertakings.

NOTE: Mississippi now has an A. PH. A. Student Branch.—See April JOURNAL, page 366.

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## PASTEUR'S TREATMENT OF HYDROPHOBIA.*

"Once more M. Pasteur has startled the civilized world with the prospect of a great discovery in medical science. He believes, and many of the greatest medical authorities believe with him, that he has perfected a method of treatment of hydrophobia which shall be not only prophylactic but, what is of far greater importance, curative also. He has for a long time occupied himself with experiments with the virus of this dreadful disease. He has kept a number of mad dogs, has obtained the poison from their saliva, and has moderated it to a safe dilution by successive inoculations on rabbits; he has "vaccinated" dogs with this modified virus, and he has proved that under the influence of the vaccination they are not, to all appearance, liable to infection. Of late he has had the opportunity of testing his solution of the virus on human beings. The discovery is still on its trial, but there can be no doubt of the great hope which may reasonably be entertained that this most terrible of diseases may not only be cured but extirpated."

* Retrospect of fifty years ago—from *Chemist and Druggist*.

# EARLY DRUG STORES IN OKLAHOMA.*

BY LOYD E. HARRIS.[1]

When was the first drug store established in Oklahoma? That question has not been answered. Oklahoma was settled in relatively small sections at a time and has been under the flags of a number of governments at various periods. It is not the purpose of this paper to review the history of the state, but some facts will be of interest.

Coronado, in 1540, together with thirty horsemen traveled through Oklahoma into Kansas and then returned through the panhandle to Texas. To the east, De Soto had sailed from Cuba and explored Alabama, Mississippi, Arkansas and possibly Missouri and eastern Kansas. This gave the Spanish claim to all of what is now Oklahoma (1).

The French came to this territory after Sieur de Bienville founded New Orleans in 1718. From that point, traders came into eastern Oklahoma and some probably went up Red River and across the plains of the western part of the state (2).

Oklahoma became a part of the United States as the result of the Louisiana Purchase, April 30, 1803 (3). Soon after this date President Jefferson sent several exploring parties into the acquired lands and some of them visited Oklahoma. Z. M. Pike and James B. Wilkinson, twenty-three soldiers and some Osage and Pawnee Indian chiefs, who had been to see the President, started from New Orleans in July 1804. They traveled to the Arkansas River where Wilkinson became ill. He and five men started back home, crossing that part of Oklahoma along the river (4).

Thomas Nuttall, the botanist, visited Oklahoma in 1819 with a party of soldiers who had been sent to remove some white families that had settled in what is now Choctaw County. He reported finding, in addition to the many plants, a salt works. This was on a trip up the Arkansas River to Glenn's trading house, near the mouth of the Verdigris River (5). Jacob Fowler described Bean's salt works, located on the Illinois River in 1821. The salt was obtained by evaporating the water from a salt well in huge kettles (6).

Fort Gibson was established in Oklahoma in 1824. Washington Irving visited there in 1832 and traveled through central Oklahoma with the rangers; his experiences are described in his "A Tour of the Prairies."

The Cherokee Indians, living in Georgia, made a treaty in 1817 to move west to Arkansas, between the Arkansas River and White River. They agreed to move on further west, in 1828, to seven million acres of land in Oklahoma. Many of them did not leave Georgia until 1838 when they were rounded up and brought to the Oklahoma lands. This is one of the forced removals of the Indians that is well known for the many hardships (7).

Practically all of Oklahoma had been explored by 1835, but there were few towns. The first mission was established in 1820, but records of the first drug store are missing.

Tahlequah was established as the Capital of the Cherokee Nation in 1839 (8). Walter Evans, who had married a Cherokee, opened a drug store there in 1870.

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The store was sold to a man by the name of Pendleton, who disposed of it to Poke Carter in 1888. Both of the latter had Cherokee wives. The store has been in the same location since its opening and in the same building since 1887. A Mr. Crew bought a part interest in it in 1896 and his brother bought the other from Carter six years later. They installed walnut fixtures in 1890, bringing them from Georgia to Fort Smith, Arkansas, by train and then by wagon to Tahlequah. The store is still owned by the Crews (9).

Early General Merchandise stores had drug departments. This is evidenced by an advertisement appearing in *The Cherokee Advocate*, a newspaper published in Tahlequah. The one in the issue of July 28, 1880, read, in part, as follows: "J. Thompson, Dealer in General Merchandise, Tahlequah, C. N.—A Full Stock of Drugs Always Kept on Hand." The first advertisement of a drug store in Tahlequah was found in this same paper in 1882. This read "Tahlequah Drug Store. Always on hand a full line of Drugs, Fancy Groceries and Toilet Articles. Physicians' Prescriptions Carefully Compounded at any hour, day or night. An Experienced Druggist always present" (10).

A drug store was in existence in Vinita, Cherokee Nation, in 1877. An advertisement in *The Cherokee Advocate* showed that it was owned by J. T. Cunningham and J. R. Trott, M.D. It was known as the "J. T. Cunningham and Co., Vinita, Drug Store." The same advertisement carried the information that they had enlarged their Drug Establishment and that they carried Stationery, Cigars, Fancy Candy, Tobacco, Window Glass, Putty, Paints, Perfumes, etc., also Patent Medicines and that prescriptions were filled (11).

Another early drug store of the Indian Territory was established by Charles Hokey, January 7, 1888, in Krebs. Mr. Hokey came to the Indian Territory from Missouri in 1876 and worked in the coal mines. He was issued a permit for his drug store by the Choctaw Nation, this yearly permit costing him ten dollars ($10.00). H. H. Hokey, his 16-year old son, started to work in the store in 1890. He acquired it in 1908. The store is advertised as "Hokey's Drug Store. The Oldest Drug Store in Oklahoma; Since 1888" (12).

The Cherokee treaty established what was known as the Neutral Strip. There was a drug store in Benton County, town of Benton (now Beaver County and the town does not exist) in 1888. This is shown by an advertisement in the Benton County Banner, Friday, August 3, 1888. It read "B. D. Fowler, Proprietor of Post-Office Store, Keeps constantly on hand a full line of DRUGS and Patent Medicines. A choice line of TOBACCOS in connection with stock" (13).

After much agitation by the so-called "Boomers," the Oklahoma Lands were opened for settlement by the white men. The Congress passed this act as a rider to the Indian Appropriation Bill. President Harrison issued the Proclamation on March 23, 1889, that these lands would be open for settlement on April 22, 1889. This was the first of the famous "Runs" for land in the settlement of Oklahoma. It is estimated that from 30,000 to 40,000 people came into Oklahoma on that day (14).

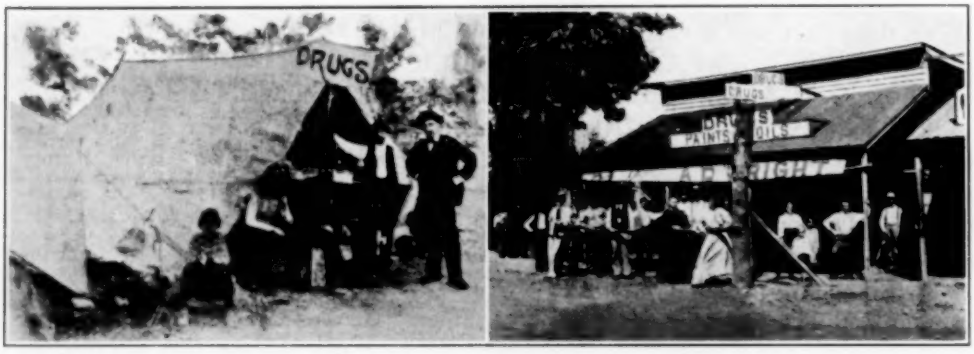
With this vast throng of people came a number of druggists. One of these was C. P. Wickmiller. He had previously been in Oklahoma, having made his earlier trip as the photographer of the Captain David L. Payne's expedition, February 1883. In this expedition there were 133 prairie schooners, over 500 men and three

women. He was finally removed from the territory by soldiers, but when he heard of the President's Proclamation, he made preparations to return.

He hired two teams and borrowed a yoke of oxen from his father-in-law. Fixtures and supplies were loaded on and he started. He arrived on time and staked the lot that has been the location of the Wickmiller Drug Store ever since. That same afternoon he put up his tent, propped up his sign "Drug Store" and did business on the day of the opening.

Mr. Wickmiller was born in Prussia in July 1858 and came to the United States at the age of five. He attended public school, at the age of six, in Scranton, Pennsylvania, and finished the course. Geography was especially interesting to him and caused him to start traveling at an early age. He is now seventy-seven years old and has been in all of the states and in fifteen foreign countries.

He registered as an Assistant Pharmacist in Kansas in 1885 and as a Pharmacist in 1886. His certificate as Registered Pharmacist in Oklahoma is number four-




Half-tone on left shows the first drug store in Chandler, Okla., started by A. D. Wright, September 22, 1891. Mr. Wright is the second man from the right, hand on tent pole. The building on the right, later, replaced the tent.

teen. He has served as president of the State Pharmaceutical Association and as secretary of the Board of Pharmacy.

Mr. Wickmiller has also taken active interest in the civic affairs of the town and the state he has helped to build. He was second mayor of his town; also, chairman of the finance committee that started the first public school and he hired the first teacher. He is a past Grand Commander of Knights Templar of Oklahoma. His collection of relics, especially Indian, and curios is one of the best private collections in the country (15).

Another of the "Runs" was the opening of the Sac and Fox territory. A. D. Wright made this run and established a drug store on September 22, 1891. He was among the early arrivals and staked a good location. He erected his tent, erected his sign and was ready for business (see picture). Mr. Wright had been in partnership in a drug store in Guthrie, Oklahoma, since late in 1889. The pictures give the development of the Wright Drug Store. He is still in business at the same location. Mr. Wright was born in Beekman, N. Y., February 9, 1863; his father was an undertaker and carriage maker. He graduated from the public schools of Beek-

man and from the Wilbraham Academy located in Massachusetts, in 1883. He came to Oklahoma in 1889 (16).

The present Greer County, Oklahoma, was a part of what is known as "Old Greer County." It was originally claimed by Texas and was organized as a County by that State in 1886. This was grass land country and part of the "Cattle Country." This land was awarded to Oklahoma by a decision of the Supreme Court, March 10, 1896 (17). The town site of Mangum, Greer County, Texas, was laid out by H. C. Sweet in 1884 (18). Dr. R. C. Hannah, a physician from Texas, came there in September 1887 and opened a drug store under the name of R. C. Hannah and Co.; his partner was Dr. H. M. Ferguson. The fixtures and supplies were freighted, overland by wagon, from Quanah, Texas. An advertisement in *The Mangum Star*, in 1898, gave the information that they were "Dealers in Drugs, Stationery, Staple and Fancy Groceries, Oils, Paints, Varnishes, Books, and Fancy Toilet Articles." A news item in the same paper read "R. C. Hannah and Co. have just put up and sold several nice buggies," and another "R. C. Hannah and Co. are now handling the celebrated Brown wagon. They have had a new supply to just arrive" (19). The picture shows some of the stock in about 1915.

A number of illustrations accompanied the article, showing periods of development. The illustration shows Mr. Wright's store in Chandler, 1915.

Dr. Hannah died in 1917 and his son, C. C. Hannah, conducted the store for about six months, when it was sold and the son went to the war. The store was reopened, in the same location, in 1933, and is being operated by C. C. Hannah.

The story of early drug stores in Oklahoma is slowly being unfolded. It is hoped that more information may be supplied from time to time.

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(2) *Ibid.*, pages 32, 33.
(3) *Ibid.*, page 50.

(4) Buchanan and Dale, "A History of Oklahoma" (1924), Chapter IV.
(5) *Ibid.*, page 64.
(6) *Ibid.*, page 65.
(7) *Ibid.*, pages 93, 106.
(8) Emmet Starr, "History of the Cherokee Nation" (1921), page 123.
(9) Private information from Jess Crew, son of one of the present owners. (Not confirmed by Newspaper.)
(10) *The Cherokee Advocate*, Tahlequah, C. N., Vol. 7, May 12, 1882.
(11) *Ibid.*, Vol. 12, July 27, 1877.
(12) Private communication from H. H. Hokey, Krebs, Oklahoma; also *The Daily Oklahoman*, October 13, 1929.
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(14) Buchanan and Dale, *loc. cit.*, Chapter XI.
(15) Unpublished Autobiography of C. P. Wickmiller; also Proceedings Oklahoma Pharmaceutical Association, 17, 63 (1905–1906).
(16) Private communication from Mr. A. D. Wright, Chandler, Oklahoma.
(17) Buchanan and Dale, *loc. cit.*, page 220.
(18) Information furnished in conversation with C. C. Hannah, Mangum, Oklahoma.
(19) *The Mangum Star*, Vol. 10 (January 26, 1898).

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## MOSES MAIMONIDES—PHYSICIAN AND AUTHOR OF MEDICAL WORKS.*

BY LOUIS GERSHENFELD.[1]

Moses Maimonides, the Hispano-Jewish philosopher, theologian, physician and astronomer, is known as Rabbi Moses ben Maimon, and (Rabbi M.b.M.) hence Rambam, often called the Second Moses and known under other names with various honorary titles. He was born in Cordova, Spain, on March 30, 1135, died in Egypt on December 13, 1204, and was buried in Tiberias, Palestine. This year marks the octocentennial of the birth of this most interesting character who is regarded as the greatest of Medieval Jewish writers, thinkers and scholars. His fame as a distinguished, and the most rational, physician of the Middle Ages was, however, overshadowed by his famous reputation as a philosopher and Talmudist.

Maimonides never attempted to employ either the Rabbinate or his scholarly attainments as a means of livelihood. Nothing in all that Maimonides ever wrote, either in his early or later days, exceeds in vehemence his denunciation of those who lived for gain by serving the Synagogue or Jewry with their learning. The teacher, the scholar, the Rabbi, like the Mishnaic sages of old, must live, he argued, by the toil of their hands, just as the layman in Jewish life, and they must not trade their holy knowledge for gain. Let it be said in all fairness that, though this may have been possible before the 14th and during the 13th and earlier centuries, changes later in Jewish life made it impossible for the teacher or Rabbi to perform the many onerous and exacting duties demanded of him, requiring as they did undivided devotion and absorbing his whole mind and heart and all of his time, unless some revenue was derived therefrom to enable him and his family to live. But the fact, nevertheless, remains that Maimonides, who by 1177 was recognized as the official head (Nagid) and Chief Rabbi of the Cairo Jews, and, in fact, of the Jewish community of

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Egypt (Ra's al-umma or al-milla), pursued his Rabbinical and intellectual career throughout his entire life without financial gain from such pursuit. After the death of his brother, Maimonides turned to medicine. He determined to utilize his medical knowledge (which he received from his studies under Rabbinical and Moslem teachers as a part of general culture) as a means of earning his livelihood; and thus, as was so frequently the case with other learned Jews, the Rabbi, the healer of the soul, became also the healer of the body. As a physician he was at first unknown; his practice was not extensive; his fame as a medical practitioner came at a much later period in his career. Accordingly, he had time to give public lectures on philosophical, Talmudic and Rabbinical subjects. Maimonides, however, never established a formal school. He spent much of his time working until the completion in 1168 of his "Sirāj" (or "Light" or "Maor" (Hebrew)) as the "Commentary on the Mishnah" was known.

The ray of sunshine in the greatly troubled life of Maimonides was Saladin. Who knows whether Maimonides would ever have risen to become the most famous Jew of medieval times and one of the greatest Jewish characters of all time had he not been Saladin's contemporary, his subject and, later, physician to his court? It was Saladin who introduced into Cairo the Medresa, or Collegiate Mosque, with its regular courses of instruction in varied fields of activities and with its free popular public lectures. When Saladin's power was supreme, he appointed the Khadi Alfadhel (or al-Qādi al-Fādil al-Baisāni), as Vizir. The latter, who (with the coöperation of Saladin's brother, el-'Adil) was practically ruler over Egypt during the last thirty years of Maimonides' life, selected Maimonides in or about 1185, as one of his physicians, alloted him an annual salary and honored him with other distinctions. Alfadhel, as his master, was devoted to culture and education and constantly fostered its promotion. Later Maimonides served as physician to Saladin and to the latter's son.

When in 1187, Western Europe heard of the fall of Jerusalem, a new Crusade was formed so as to recapture the Holy City. The details of the third Crusade cannot be told here. Suffice it merely to mention that Richard I, the Lion Hearted, King of England, was at the head of the latter. When all was over we find that Saladin remained in power and in possession of Jerusalem, which was to remain under the protection of Moslem rule and the Crescent until its capture during the recent World War. In his conquest he was aided by his brother el-'Adil and it was the latter who served as the intermediary between Saladin and King Richard. It may have been that el-'Adil, who later was regarded as the Sultan of Egypt, related the wonderful deeds of Maimonides to King Richard and that Richard may have sought his service as his private physician, an honor which is said to have been declined by Maimonides. If the latter actually received such a request, or if Richard, the Lion Hearted, asked Saladin for his physician, Maimonides more than likely must have or would have declined, as it undoubtedly must have appeared to him unwise to leave a Moslem saint for a Christian brute and savage.

Maimonides practiced medicine with religious fervor, as if the medical art was a holy calling. He himself tells us that the purpose of medicine "was to teach humanity the causes of ill health, the correct dietetic hygiene, the methods of making the body capable of useful labor, how to prolong life, and how to avoid disease. It thus directly elevates the human being to a higher moral plane where the pursuit of

Truth is possible and where the happiness of the Soul is attainable." Those interested in preventive medicine can gather much of interest in Maimonides' writings, for hygiene (and especially dietetic hygiene) is a topic discussed freely and frequently in many of his works. He was a staunch advocate of the guarding against, rather than the curing of, disease.

His extensive medical knowledge was sought by the court and the general population alike. He was admired by the élite, worshipped by the masses and was the favorite of royalty and the idol of their subjects. In one of his letters written in 1199 to his disciple Samuel ibn Tibbon advising him not to visit him at that time, he gives a vivid picture of his professional duties which required all of his time, day and night, so that he had but little freedom for himself, even for his meals. In spite of these duties, he still fulfilled the functions of Chief Rabbi or Nagid and wrote "Responsa" addressed to all parts of the world. His energy was invincible. The following extracts from this letter are of interest:

"Now God knows that in order to write this to you I have escaped to a secluded spot, where people would not think to find me, sometimes leaning for support against the wall, sometimes lying down on account of my excessive weakness, for I have grown old and feeble. I dwell at Fostat and the Sultan resides at Cairo. These two places are two Sabbath days' journey (about one mile and a half) distant from each other. My duties to the Sultan are very heavy. I am obliged to visit him every day, early in the morning; and when he or any of his children, or any of the inmates of his harem, are indisposed I dare not quit Cairo, but must stay during the greater part of the day in the palace. It also frequently happens that one or two of the royal officers fall sick, and I must attend to their healing. Hence, as a rule, I repair to Cairo very early in the day, and even if nothing unusual happens, I do not return to Fostat until the afternoon. Then I am almost dying with hunger. I find the antechambers filled with people, both Jews and Moslems, nobles and common people, judges and bailiffs, friends and foes—a mixed multitude, who await the time of my return. I dismount from my animal, wash my hands, go forth to my patients, and entreat them to bear with me while I partake of some slight refreshment, the only meal I take in the twenty-four hours. Then I attend to my patients, write prescriptions and directions for their various ailments. Patients go in and out until nightfall, and sometimes even, I solemnly assure you, until two hours and more in the night. I converse with and prescribe for them while lying down from sheer fatigue, and when night falls I am so exhausted that I can scarcely speak. In consequence of this, no Israelite can have any private interview with me except on the Sabbath. On that day the whole congregation, or at least the majority of the members, come to me after the morning service, when I instruct them as to their proceedings during the whole week; we study together a little until noon, when they depart. Some of them return, and read with me after the afternoon service until evening prayers. In this manner I spend that day. I have here related to you only a part of what you would see if you were to visit me."

All of his medical writings were written in Arabic. Though these contain summaries, classifications and elaborations of Galen's writings derived in the main from the standard Arabic Galenism of his day (from such authors as al-Razi (Rhazes) (born about the middle of the 9th century; died 923 or 24), al-Tamīmī, Ibn Sīnā (Avicenna) (980–1037), Ibn Wāfid, (997–1074), 'Ali ibn Ridwān (998–1061 or 1067), and Ibn Zuhr (Avenzoar) (1091 or 94–1161 or 62)), they are tempered with his own critical knowledge gained through his extensive experience by direct observation and by actual experimentation. His most popular medical work, generally spoken of as Moses' Aphorisms or Moses' Medical Aphorisms or Principles, was the Kitāb al-fusūl fī-l-tibb or Fusūl Mūsā, (known in Hebrew as Pirqe Mosheh), written about 1187–1190. It is a collection of 1500 aphorisms extracted from

Galen's writings, together with 42 critical remarks. Galen's thoughts were classified in 24 chapters devoted respectively to:

Chapters (1–3), anatomy, physiology, general pathology; (4–6), symptomatology and diagnosis, with special reference to the pulse and urine; (7), etiology; (8–9), general and special therapeutics; (10–11), fevers and crises; (12–14), bloodletting, cathartics, emetics; (15), surgery; (16), gynecology; (17), hygiene; (18), gymnastics, massage, etc.; (19), bathing; (20), dietetics; (21–22), drugs; (23), Galenic ideas which are often misunderstood; and (24), rare cases. In a final chapter (25), the author outlines a general criticism of Galenic medicine and philosophy, indicating some forty topics about which Galen contradicted himself. It ends with a discussion of Galen's teleological ideas from the Biblical standpoint. This last chapter, the most important of the work, was apparently unfinished at the time of Maimonides' death, as it was edited posthumously by the latter's nephew, Yūsuf ibn ʿAbdallāh Abū-l-Maʿālī, in 1204–1205.

Next in popularity only to the Fusūl was the Māqāla fī-tadbīr al-sihha, known popularly as the Tadbīr al-sihha:

This is composed of four books on diet and personal hygiene and was addressed about 1198 to al-Mālik al-Afdal Nūr-al-dīn ʿAli, Saladin's eldest son. The latter suffered from fits of melancholia, and requested from Maimonides, his chief physician, a regimen. This work, a compilation obtained from ancient and Arabic writings and published first in Hebrew in the Journal "Kerem Hemed" (III, 9–31), is divided into four parts, as follows: (1) explanations of the case, and general hygienic and dietetic rules, with frequent references to Hippocrates and Galen; (2) easy remedies for use while traveling, or when a physician is not available; (3) hygiene of the soul; psychotherapeutic rules partly derived from Aristotle and from al-Fārābi; (4) summary of hygiene and dietetics in the form of seventeen aphorisms. The Tadbīr al-sihha, or Maimonides' work on personal hygiene and dietetics, is of interest from many viewpoints. Therein, with bitter sarcasm and much irony he deplores the low and degraded state of the medical profession during his time and the apparent success of various charlatans and bragging healers. He stresses the necessity and importance of a detailed and thorough professional training for medical practitioners, and also the need of careful personal attention to one's patients. Details are given concerning the relation between the patient and his physician, and vice versa. Of interest is his statement that slight indispositions may, whenever possible, be treated without any special help of physician or drugs; but a catarrh, he warns, must not be taken too lightly. Though Galen and Hippocrates are frequently quoted in this work, he gives his own views on personal hygiene and dietetics, which are of interest. In this work as well as in others, one finds that his whole theory of health is thus condensed into two brief rules: "A man should not eat too much, nor should he give up exercise." He constantly warns against satiety and overloading the stomach. Among some of the thoughts promulgated and rules given in this treatise as useful for the preservation of health, the following excerpts are of interest:

"If a person took as good care of himself as he does of his domestic animal, he would avoid many diseases. No one throws food to his animal without measure, but he feeds it in accordance with its needs; yet he himself consumes food without any measure or control. One should also take into consideration the moving around of domestic animals and the exercise they get lest they become stiff and perish. He, however, does not do that with himself and neglects exercising his body, which is the greatest support of good health and a ward against many diseases." In speaking of physical exercise, he continues: "We have mentioned the saying of Hippocrates: 'Continuation of good health depends on being careful of sluggishness.' Indeed, there is not a thing that could take the place of exercise; for with exercise the natural heat gets inflamed and all waste matter is thrown off, whereas inertness extinguishes the fire of the natural heat, and the superfluities of the body are not thrown off, 'but not every movement of the body is considered by physicians as exercise.' Only a vigorous or quick movement, or both combined, could be termed exercise. It is with the vigorous movement, resulting in change of breathing, that the person begins to breathe deeply. A movement stronger than that brings about a fatigue, *i. e.*, a very strong exercise causes fatigue, which not every one is able to stand, and there is no particular necessity in that, the most beneficial for the preservation of health being the brief exercise."

"One should exercise on an empty stomach only, and after the excrements are thrown off

(urine and bowels). Likewise, exercise should be avoided in excessive heat and excessive cold; the best time for it is early in the morning after one gets up from his sleep and throws off the excrements. To the general principles for the preservation of good health, promulgated by Galen, belongs the following: 'Just as movement before eating is altogether beneficial, so is movement after eating quite injurious.' By this is meant the avoidance of heavy exercise after eating as well as coitus and bath, which are very harmful, especially to those who naturally have thin and narrow veins. Yet it is advisable to move around lightly after meals from one end of the room to the other until the food is well settled in the stomach and rests there until digested. Sleep helps digestion, especially with those who are in the habit of sleeping in the day time."

In his opinion the best of sports are throwing a ball and wrestling. Old men should not fail to go in for physical exercise of some kind. Maimonides details the quality of different foodstuffs, and warns against the use of food which has begun to deteriorate. He recognizes that milk may affect individuals differently and in speaking of milk products he says: "Fresh milk is a good food for those in whose stomach it will not sour, nor ferment, nor form flatulence in the region below the loins. Galen recommends that one should add to the milk a little honey and a pinch of salt, so as to avoid its curdling in the stomach. The best kind of milk is the tenderest, such as milk of goats, or of she camels, which is also good. Whatever is prepared from milk or is mixed with it is very unhealthy, such as curdled milk, sweet or sour milk mixed together and whey. Likewise all that is cooked of milk and in milk is unwholesome as food. Cheese is a poor and heavy food, except the fresh white cheese which is sweet of taste and contains little fat. Galen praises it as a nourishing food. Other kinds of cheese are objectionable, especially the old cheese containing much fat. Fresh and melted butter is not a bad food for anybody." On the whole, Maimonides warns that one should be careful in the selection of fresh fruit which is to be consumed. This is perhaps due to the fact that many infections prevailed during the early days when eating raw fruits and vegetables not washed or cooked properly or peeled. He says: "Vegetables which generally are not wholesome as food are garlic, onions, leek (related to the onion), radishes, cabbage and egg plant; and people who take care of their health should avoid them. Cantaloupe is easily digestible, when eaten the first thing in the morning on an empty stomach, having no flow of bad secretion and not containing any bad mixture. It has then a slight cooling effect on the body, throws off the urine and cleans the veins of impurities, it being thus a wholesome food. I have mentioned it here, for it is used much by people."

"In regard to fresh fruit it is well to know that whatever grows on trees cannot be generally recommended as food. Yet some fruit is not as bad as others: so carobs, fruit of the lotus tree, and the medlar are quite wholesome, whereas figs and grapes are not nearly so bad, in fact almost wholesome, as Galen speaks of figs and grapes as chiefs to all fruit. They are, indeed, the least injurious, yet one should not overtax the blood which is required for digesting all fruit (*i. e.*, one should not eat too much of this fruit). My statement that whatever grows on trees cannot be recommended as food must not be misunderstood, in view of the fact that fruit juices as well as sirups and confections prepared from fruits are beneficial as medicine in various diseases, for the virtue of foods as food is different from their virtue as remedies for diseases; this is quite evident to those versed in the medical art."

"There is a statement of Galen in which he offers a solemn advice to people that they should not eat any fruit. He says that every year he used to suffer from fever, then following his father's advice completely to abstain from eating fruit, and since then up to the time he wrote his treatise, he suffered from fever only one day. The fact that many people eat these fruits yet do not suffer from fever is no proof to the contrary, for change in habits and variety in dispositions bring about different rules. If the Hindu, *e. g.*, ate well-prepared bread and mutton meat he would surely become ill, and, on the other hand, if one of us limited his diet to rice and fish as the Hindus do, he would likewise become ill. However, the purpose of this treatise is not to cite the causes thereof, but its aim is that we know that, generally speaking, fruits are not wholesome and should be eaten in moderate quantity. They must not be mixed in any form with other foods. Fruits that act as laxatives, such as plums, grapes and figs, are to be consumed before the meal which is to be taken only after the former is emptied from the stomach, whereas those that act as astringents as quinces and pears, should be taken after meals in moderate quantities, as much as to have their fragrance in the stomach. Just as figs and grapes are the best of fruits, so are peaches and apricots the worst among them. The latter two cannot be digested at all, an ap-

preciable quantity of waste matter remaining in the veins mixed with the blood, where it eventually boils, thus causing the inception of putrid fever."

"Dried fruits, such as raisins, dried figs, kernels of pistachio nuts, kernels of dry almonds, are not unwholesome; however, they are recommended as beneficial after meals, especially raisins and pistachio nuts, which are very good for the liver; and 'A healthy liver is our life,' as Galen said. In a similar manner it is good to take a little of sweet dessert after the meal in order to enable the stomach to envelope the food and digest it properly." His Maqāla fīl-l-bayān al-ā 'rād (Discourses on the Explanation of Accidents) regarded by some as the continuation of section five of his work on diet, was written for the same prince al-Afdal, who was then residing at Riqqua in Upper Egypt. This work, known in Hebrew as Teshubot 'al she 'elot peratiyyot and in Latin as De causis accidentium apparentium, is divided into 22 chapters. Written about 1200, it apparently was Maimonides' last medical effort. Therein are contained many prescriptions, formulas of other physicians, with his own criticisms gently expressed; and prescriptions by himself follow, which are of interest because of their simplicity and medicinal value.

Maimonides' work on poisons and antidotes, Kitāb al-sūmūm wal-mut'aharriz min al-adwiya al-quitālah, was written in 1199 for and at the request of the vizir al-Qādī al-Fādil, and is also known as the Risālat al-fādilīyya. It was translated into many languages. The Latin translation known as De venenis (or contra venena) was a text extensively used by fourteenth century physicians. The Hebrew translation is known as Ha ma' amar ha-nikbad (or Ha-ma'amar beter 'iaq). This work, a compilation of all that was known about the subject treated, is divided into two sections, preceded by an introduction, the latter explaining al-Fādil's efforts to obtain from many distant countries all the ingredients needed to prepare the great theriaca. Section I, divided into four parts, deals with the venomous stings of insects, (scorpions, spiders, bees, wasps, snakes, etc.), the biting of mad dogs and the treatment of such wounds. He points out the great length of time of the incubation period of rabies, and he states that the bite of a mad dog is to be feared, whereas that of a healthy dog is of little importance. Section II, divided into six chapters, deals with vegetable and mineral (mainly internal) poisons (such as verdigris, arsenic, litharge, opium, henbane and other solanaceous herbs, mushrooms, etc.), and their antidotes. The clinical description of some cases of poisoning are very interesting. In this work, Maimonides constantly mentions the necessity for ligation and suction of wounds. Here in part are directions which he gives for the treatment of poisoned wounds: "The first thing to do is to apply a tight band above the bitten part so as to prevent the poison gaining entrance to the body. While this is being done, an assistant should make incisions in and about the wound, and then, after rinsing one's mouth with oil, or with oil and wine, the wound should be thoroughly sucked, being careful to spit out everything taken into the mouth. He who so sucks the wound should have no sore places in the mouth, nor any carious teeth. Should sucking be impossible, cupping may be resorted to." General instruction for relieving pain by local applications and the use of remedial agents as stimulants (if necessary) are given. Much of this practical aid is used to-day while waiting for specific serum (antivenin) to arrive and to be injected.

Two treatises, short and long texts, were written by Maimonides on coitus and on the hygienic aspects of sexual intercourse. This work, the Maqāla fī-l-jimā' was dedicated to al-Muzaffir I, (Ayyubid) Sultan of Hamāt (1178–1191), nephew of Saladin. The Hebrew translations are known as Ma' amar 'al ribbui ha-tashmish and Ma-amar ha-mishgal. The longer text is divided into 19 chapters and deals with differences in sexual temperament, the use and danger of sexual intercourse, abstinence, aphrodisiacs and anaphrodisiacs, narcotics, etc. Regarded as an authority during his day, and an advocate of sexual intercourse, the following extract is of interest "Copulation is life; strength to the body, and light to the eyes. But when one abuses it, the body is consumed in its vigor and life is crushed. Solomon has well said in his wisdom: 'Give not your strength to women.'"

The Maqāla fi-l-rabw (a work on asthma), written about 1190, contains 13 chapters dealing with diet and climate in general, with a discussion of the climate and food of different countries, particularly of Egypt. The best diet and climate for asthmatics follow. His treatise on hemorrhoids (Māqala fi-l-bawāsīr), known in Hebrew as Ha-ma 'amar bi-refu 'at ha-tehorim, is composed of seven chapters. He ascribed hemorrhoids to bad digestion, mainly to chronic constipation, and advocated a light diet, predominantly vegetarian. Mild purgatives, enemas and laxatives are described. He mentioned the danger of bloodletting, describes a method of drying up

hemorrhoids by vapor treatment and in considering surgical intervention, he says that this should be reserved for extreme cases. His thoughts concerning bloodletting reveal them to be ahead of his time. Though advising against this method and stating that it should not be employed for children and very old people, he presents the conclusion that it should not be the age of the patient which should decide the practice of this technique, but its use should be governed by the general physical condition of the patient.

A collection of extracts from Galenic writings, the Mukhtasarāt (abridgements, digest) (lost in its original Arabic but available in Hebrew translations) and a commentary on Hippocrates' Aphorisms, are to be found among his medical works. Other medical writings ascribed to him are the Sefer-refu 'oth (Book of remedies or medicines) in Hebrew, and the Kitāb al-asbāb wal-'alāmāt (Causes and Symptoms) in Arabic. It is of interest to note that in his many writings on methods of treatment he reveals a marked opposition to polypharmacy (complicated mixtures of medicaments). He recommends only simple remedies and would only use drugs which he himself tested or which had been found satisfactory and in turn recommended by recognized medical authorities. "In minor ailments," he wrote, "Nature cures the body without the need of medicinal remedies, if the patient only follows certain dietetic regulations. Where, however, the services of a physician are required, he should see to it that he aids Nature in her beneficial course. Most of the doctors err in their treatment. In endeavoring to assist Nature, they weaken the body with their prescriptions."

The Physician's Prayer, ranking as it does with the Oath of Hippocrates (matching the latter and completing it from the Jewish viewpoint), has been widely circulated and is a valuable contribution to medical deontology. It is ascribed to Maimonides and is most frequently known as Maimonides' prayer. However, there is no genuine proof that this was composed by Maimonides, though many regard it as Maimonidean in tone and spirit.

Brief comments should be made here of the three of his greatest works, a triology. Though they are included among his Rabbinical and philosophical writings, information concerning medical subjects are to be found therein. His first great work was the Sirāj (or Light (or Maor Hebrew)) or his Commentary on the Mishnah. "A physician," he says in this Commentary on the Mishnah, "should begin with simple treatment, trying to cure by diet before he administers drugs." It is of interest to note that in his "Responsa" he applies this principle to spiritual ills as well. The following opinion voiced almost 800 years ago by Maimonides can be aptly applied to-day: "Like unto a murderer," he wrote, "is the physician who refuses to tender his assistance in time of necessity, or who practices without undue study of the ailment which he is treating." Maimonides warns individuals against marriage with any one from the family of a leper or epileptic, or one incapable of propagation. He states that a healthy man needs, on the average, eight hours of sleep. He should get up early, best of all before sunrise. He warns changing a habit suddenly, or he will fall ill, and he states: "If a habit is pronounced bad for a patient and is to be given up, it should be done gradually. Drastic cures ought never to be undertaken alone, but only under the supervision of a physician."

The Mishnah Torah or Double of the Torah (Repetition of the Law; Deuteronomy) or Strong Hand (YaD ha-Hazaqah) (Sefer ha-yad), (written in new Hebrew not Hebrew-Arabic) is the first complete digest, classification and codification of all the Mosaic and Rabbinical laws. It is enriched with much of his own philosophical and scientific thought and contains material derived by industrious work and compilation not only from the Torah and from both Talmuds, but also from the Geonim, the whole consisting of 1000 chapters being classified in fourteen books or sections. In this work, one finds the whole of Jewish jurisprudence, religious, civil and criminal, astronomical knowledge and medical information, coupled with a considerable amount of general data and philosophical thought. It is difficult to appreciate the significance of this masterful and gigantic work. Regarded by many as the greatest work in Jewish literature after the Bible, it has obtained a semi-canonical status in Israel.

The most famous work written by Moses Maimonides and which crowned his reputation, was the Dalālat al-Hā'īrin, or Guide for the Perplexed, or Moreh nebukim (Hebrew), (or Doctor perplexorum), completed in 1187–1190. Written in Arabic, the original text was given in Hebrew characters. Translations in French, Hebrew, Latin, Italian, German, Spanish and in English are available. A better translation of Dalālat is guidance; and "A guidance for the perplexed" is what Maimonides intended this work to be. This treatise appeared in the form of letters ad-

dressed to his disciple Josef ibn 'Aknin, and was sent to him chapter by chapter as Maimonides completed them. It was not intended for the multitude or the masses, but it was written from a philosopher to the philosophically inclined (to the select). He attempted to bring mental peace and spiritual comfort to the "perplexed" and the result was his "Guide." His purpose of this work was to reconcile faith with reason, to reconcile Aristotelian philosophy and thought with Jewish theology and the doctrines of Judaism. This was something new, something original, something never attempted before by any Jewish thinker. To some extent he championed science against the fundamentalism of the Bible, though he was at all times honest and consistent in the belief of the truth of the Aristotelian system and convinced of the truth of the Mosaic doctrine and of the Divine origin of the Torah. Though much can be said pro and con for this and other of his works, at least Maimonides must be credited with the fact that he pointed out that philosophy and science did not begin nor did it end in the Scriptures and Talmud. Of interest is Maimonides' comment in this work concerning wine. One must remember that this and other spirits were forbidden the Arab by his religion. Though in a dilemma, he mentions its useful and wholesome properties: "He who is careful concerning it (wine) will be called a saint; wine in early and later days has driven many to perdition. He is wrong who believes that to be drunk once a month is useful. A youth under 21 should never touch wine. The older a man gets, however, the better wine is for him, and the very old need it most. Wine in small quantities is good for digestion; it is a tonic, even a remedy for many diseases. It does away with heavy, melancholy thoughts, and induces good sleep."

## LOUISVILLE COLLEGE OF PHARMACY STUDENT BRANCH.

The regular monthly meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION Student Branch of the Louisville College of Pharmacy was called to order on April 1st at 2:30 P.M. by President Wm. J. Walsh. All members were in attendance.

The minutes of the March meeting were read and approved. The treasurer reported a balance on hand of $21.70.

The special program consisted of two papers, ably prepared and presented by Fred P. Kranz, Jr., on "Phenol" and by Claude M. Lloyd on "The Official Remedies for Burns." A discussion of the papers followed.

The Program Chairman, Horace Hannon, announced that Dr. Virgil Simpson would be the speaker for the May meeting. Motion was made and carried that the entire student body be invited to attend the May meeting and also to invite the Kentucky A. PH. A. members to attend.

JOE BLACK, *Secretary.*

## COMPLETE DRUG STORE PRESENTED TO TEMPLE UNIVERSITY.

A complete model drug store has been presented to the Temple University School of Pharmacy by Sharp and Dohme. Presentation of the store was made by President J. S. Zinsser, who said he hoped it would be dedicated "to the promotion of professional and ethical pharmacy, and also the means of a better approach to the practice of professional pharmacy."

The model store will be used as a background for the practice of professional pharmacy. Dr. Charles E. Beury, president of Temple University, accepted the store in behalf of the University. He also thanked Dr. H. Evert Kendig, dean of the Pharmacy School, for his efforts in securing, planning and installing the store.

## MISSISSIPPI PHARMACY BOARD NAMED BY GOVERNOR.

The Mississippi State Board of Pharmacy, selected from nominees proposed by the Mississippi State Pharmaceutical Association, was appointed by Governor Hugh White: Kelly Patterson, of Jackson; J. J. Gerache, of Vicksburg; Lew Wallace, of Laurel; W. H. White, of West Point, and T. H. McMillion, of McComb.

The 84th Annual Meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION will be held in Dallas, Texas, August 24–29, 1936. Hotel Adolphus, Headquarters.

Conferences, Sections and Committees note that the time for the meeting is fast approaching.

# THE DEPARTMENT OF THE AMERICAN ASSOCIATION OF COLLEGES OF PHARMACY

C. B. JORDAN—CHAIRMAN OF EXECUTIVE COMMITTEE, A. A. C. P., EDITOR OF THIS DEPARTMENT.

The value of placement tests, such as are usually given during the orientation period to students entering college, depends upon the intelligent use that is made of them. Some instructors believe that they are of little or no value and therefore cast them aside. Others place too much confidence in them as indicators of the progress that a student should make in college. The wise instructor is willing to withhold judgment until he has determined the correlation (or lack of correlation) between the results of these tests and the work that a student does in college. The following papers by Drs. McMurray and Lee give their results of such a study. Therefore, these papers should be of considerable interest to any instructor who is endeavoring to make use of placement tests.—C. B. JORDAN, *Editor*.

## THE 1935 COLLEGE OF PHARMACY ENTRANT.**

BY R. L. MCMURRAY.*

Within and without the ranks of Pharmacy[1] questions continually confront us as to how we are keeping pace commercially, professionally and educationally with contemporary fields. Commercially you know the answer. Drug stores in 1933 marketed[2] $1,066,252,000.00 worth of products. Professionally you know the answer in up-to-date apothecary shops, hospital pharmacies, synthetic remedies and general scientific progress. But few know how the College of Pharmacy has progressed in its determination to graduate a better pharmacist.

After the World War there was a rush into education of returned soldiers, government employees and others, who had, for various reasons, deferred their education. In addition the enrollment included students of normal age, but who had attended school during the influenza epidemics and the general hysteria more or less prevalent to that war period. At that time the common trend was to choose the two-year course in Pharmacy and rush back to the retail business. Thus, the pharmacy student body for a period of more than five years following the War was composed of an extraordinary lot of individuals.

About the time of the World War new methods for testing the student's mental ability became the chief interest of a certain group of educators. All students in the University were subjected to intelligence tests—otherwise known as the "nut tests." And while the size of a Hottentot may not have any direct bearing on the proper method to prepare an emulsion of cod liver oil, nevertheless the results of these tests were not flattering to the relative standing of pharmacy students as compared with students in the other colleges of the Ohio State University. I am still very much conscious of the shock experienced during my freshman year when in the dean's office for the first time. There I noticed that the results of the intelligence tests had been plotted on a chart and that the College of Pharmacy students had the lowest intelligence rating for any group of students in the Ohio State University.

* College of Pharmacy, Ohio State University.

** Presented before meeting of Boards and Colleges of Pharmacy of District No. 4, 1936.

[1] *Drug Topics*, 51, No. 43, 17 (1935).

[2] U. S. Dept. of Commerce, Census of American Business: 1933 (May 1935), 7.

The direct result of graduating these students from the College of Pharmacy has been an overproduction of registered pharmacists with subsequent deleterious effects upon the general tone and morale of pharmacy. Unregulated overproduction tends to follow economic laws. The hours of work were lengthened and the wages decreased until many self-respecting men refused to engage any longer in retail pharmacy work. Many left the retail pharmacies. I know of many who turned to other fields—and they are not second-rate men either. For instance, one man who graduated in 1925 is now advertising manager for a large unit of a newspaper chain in a town of 400,000 people. Another registered pharmacist is a successful house-painting contractor in a town of 50,000.

To-day the cry and demand of Retail Pharmacy is for protection. In the education branch of pharmacy this cry has not come to stoppered ears, but a College of Pharmacy functioning as a unit of a state-supported university must offer its services unbiased to all who apply in a regular manner for admission as students. Therefore, the College of Pharmacy at Ohio State University has been limited in the matter of selecting students for it must constantly bear in mind that the spirit of education in the United States is equal opportunity for all. However, the graduating of a capable type of student will add very much to the protection that pharmacy is seeking to obtain. There are a number of factors in the retail business that might be non-desirable but the elimination of these factors cannot be accomplished over night. In some cases the student of to-day will be the one who will eventually carry on the fight. Therefore, if the college attracts and educates the very best graduates of the high school then it has furnished the essential material for bettering Pharmacy, for no profession will ever rate above the members composing its body.

A tabulation has been made of entering students at the Ohio State University in the fall quarters of 1924, 1925, 1934 and 1935. The last year for admittance into the two-year course was 1924. The state laws require that the Ohio State University accept all graduates of accredited high schools within the state. Therefore, the student body cannot be selected as private schools do. However, the course of study could be lengthened and this was done, with gratifying results, as herewith shown. The figures for these two sets of years follow.

In the autumn of 1924, 119 students were admitted into the College of Pharmacy, of whom 2.52% were in Class I, 12.6% in Class II, 52.81% in Class III, 21.08% in Class IV and 10.92% in Class V. Ten years later, in the fall of 1934, 50 students were admitted, of whom 8% were in Class I, 24% in Class II, 60% in Class III, 8% in Class IV and 0% in Class V. In other words, there was an increase of 16.88% of students in the upper two ranks in the year 1934 over the year 1924, based on the results of the intelligence tests.

In the following set of years, 1925 and 1935, the same improvement was noted. In 1925, 60 students were admitted, of whom 5% were in Class I, 11.66% in Class II, 45% in Class III, 25% in Class IV and 13.33% in Class V. Ten years later, 1935, 63 students were admitted, of whom 11.11% were in Class I, 23.8% in Class II, 58.73% in Class III, 3.17% in Class IV and 3.17% in Class V, thus showing an increase of 18.25% in the upper two classes over 1925.

These figures are summarized from the results of the intelligence tests. They indicate what the student is supposed to be able to do.

There is another way to measure the student, and consequently the pharmacy student. That is by the grades made in high school and relative standing in the high school class.

In the autumn of 1935 the College of Pharmacy at Ohio State University accepted 48 students who had no previous college training. Transfer and reinstated students were excluded from this study. The high school records of the applicants were examined and classified into thirds on the basis of high school achievements. This classification was made by an impartial committee working under the direction of the University Entrance Board. This same committee appraised the merits of all applicants for all the colleges in the University. It was found in studying the records of the pharmacy students that only 12.5% were in the lower third, 41.66% in the middle third and 45.83% in the upper third. Thus when the pharmacy freshmen of 1935 were studied in relation to all the other students admitted to Ohio State University it was found that the college was getting three times as many upper third students as there were in the lower third group.

Again, a study was made of our freshmen pharmacy students in relation to the total number of graduates from high schools represented. Thus, this study was made on figures pertaining not only to students who gained admission to Ohio State University, but to the entire remainder, whether they went to some other college or whether they discontinued school. Because of incomplete data filed, the basis of this study was limited to 28 students. By the same method of grouping it was found that 10.71% were in the lower third of their high school class, 32.14% in the middle third and 57.14% in the upper third of a total of 3680 students in the graduating classes of the high schools represented. In other words the majority of the freshman class of 1935 came from the upper third of their high school class.

It is unfortunate that the present system of entrance credentials was not used during past decades. This lack of data has prevented a comparison with students of former years with the degree of accuracy obtainable for the period just studied.

The conclusion to be reached from a study of these entrance statistics must be made after giving due consideration to the changes in the curriculum of the College of Pharmacy in the 12-year period. The last year for students to be admitted in the two-year course was 1924, and thereafter the four-year course only was in effect. Therefore, this is probably the earliest that a check could be made to determine the benefit to be derived from the higher academic requirements. These changes, plus more adequate quarters and a constant study of newer and better methods in use throughout the profession, lead the faculty of the College of Pharmacy at Ohio State University to believe that a better class of students is being attracted to the profession of Pharmacy, and that the four-year course has been of marked benefit in this respect.

## OUR EDUCATIONAL LOSSES.*

BY C. O. LEE.[1]

In the fall of 1926, Purdue University gave orientation examinations, for the first time, to all the freshmen coming into the University. These tests were eight

* Presented before meeting of Boards and Colleges of Pharmacy of District No. 4.

[1] Professor of Pharmacy, Purdue University.

in number, divided into three main groups as follows: *First*, general ability tests including intelligence examination and the "Purdue Reading Test, Comprehension." The second group included subject matter ability tests under which were given, Chemistry Aptitude tests, Mathematics Aptitude tests, Physics Aptitude tests and English Aptitude tests. The third group included subject matter training tests under which were the English Training Test and Study Outline Test. Since that time the number of tests has been reduced to the following four: Chemistry Test, Purdue English Test, Psychological Test and Mathematics Training Test. It should be stated that the present chemistry test is for those students who have had chemistry and is given for purposes of classifying the freshmen in the chemistry courses. Since all pharmacy students are required to enroll in the beginning chemistry courses, irrespective of their previous knowledge of the subject, they are not required to take the examination. In reality, then, our freshmen are required to take but three entrance examinations.

During these ten years the students of the School of Pharmacy have taken these tests along with the other entering students. We have watched, with considerable interest, the results of these examinations and tests. As instructors of these students, we should not be too greatly influenced by the results of these examinations for two reasons. The first is that it has become a sort of tradition about the campus that high scoring students are expected to do more and better work than those of low scores. Those who take the suggestion seriously might make an unjust score for themselves and be wrongly classified and in turn misjudged. The second is that the instructor, in looking over the records, might easily be influenced either against or in favor of the student. We have tried not to allow the results of these examinations to influence our judgment or feeling with respect to the student until we have had him in class for a considerable number of weeks. After we have become acquainted with the student and then find that he is doing rather badly in his work, we may refer to the examination records to see whether the student has ability, according to these tests, to carry on the work that has been assigned to him. I sometimes resort to them to help clear up my questionings with respect to certain students. If I find that their work has been unsatisfactory and that their test records show that they were low ranking students, I feel more confident in passing judgment as to whether they should be allowed to continue the course or be advised to drop it. This again is a bit dangerous because we have had a number of students with comparatively low orientation records, yet possessed with certain qualities of determination and willingness to work, who have made very desirable records. On the other hand, we have had students enter with splendid orientation records who, because they lacked these qualities, have been failures, or at least have not been very successful students.

In looking over our records of entering students for the past ten years and checking the number who have entered against those who have graduated, we find a very decided loss in the number who have been able to carry through the four years required at the University. This naturally causes us to ask ourselves, what has happened to these students who have fallen by the wayside? Perhaps we should not be too greatly concerned about our losses, yet it would seem that it is a problem worthy of some consideration. It is rare that we graduate as seniors more than 50% of the entering freshman class. We know considerable about those men

who have stayed with us through the four years and have become rather well acquainted with them during their college careers. Those, however, who remained with us one, two, three and sometimes as long as four semesters, and then dropped out of the University, were soon lost from our knowledge. This report is an account of those students who came to us as freshmen, and a record of what happened to them in the University. It is interesting to note that some stayed for a few weeks, some a few months, some as long as two years and then dropped out of sight and we have not heard from them since. Should we be concerned about them? It seems that we should, because without doubt a number of students who have dropped out for financial causes, or failure in grades, might well have been saved. A number of people who have had their college careers cut short for various reasons might have proved to be very good students and worthy of graduation.

### STUDENTS AND THE RANKING GROUPS.

From the records the entering students have been classified with respect to the results of the examinations given them into decile groups and I have shown the number of each class that fall into the various deciles from the lowest to the highest. The School of Pharmacy of Purdue University from 1926 to 1936 has had 448 students enrolled. These are all shown in Table I, which follows. It is interesting to note that 73% of our students fall in the lower five decile groups and only about 26% are included in the upper five groups. Again it will be seen that about 41% of our students fall into the three lowest decile groups and only about 10% of them in the three highest decile groups.

TABLE I.—DECILE GROUPS.

| Year. | 1–10. | 11–20. | 21–30. | 31–40. | 41–50. | 51–60. | 61–70. | 71–80. | 81–90. | 91–100. | Misc. | Total. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1926 | 4 | 6 | 15 | 8 | 7 | 4 | 9 | 2 | 1 | 0 | 4 | 60 |
| 1927 | 2 | 5 | 7 | 12 | 8 | 5 | 3 | 1 | 3 | 2 | 1 | 49 |
| 1928 | 8 | 6 | 10 | 9 | 9 | 2 | 3 | 3 | 1 | 1 | 3 | 55 |
| 1929 | 5 | 7 | 4 | 6 | 3 | 2 | 3 | 4 | 0 | 0 | 0 | 34 |
| 1930 | 3 | 5 | 3 | 6 | 3 | 5 | 5 | 4 | 1 | 0 | 0 | 35 |
| 1931 | 4 | 8 | 4 | 4 | 5 | 3 | 2 | 2 | 0 | 1 | 0 | 33 |
| 1932 | 1 | 7 | 8 | 5 | 4 | 3 | 1 | 3 | 1 | 0 | 0 | 33 |
| 1933 | 1 | 3 | 7 | 3 | 11 | 4 | 2 | 3 | 3 | 0 | 0 | 37 |
| 1934 | 5 | 8 | 9 | 2 | 12 | 4 | 3 | 1 | 1 | 0 | 0 | 45 |
| 1935 | 13 | 7 | 6 | 11 | 13 | 4 | 6 | 6 | 1 | 0 | 0 | 67 |
| Totals | 46 | 62 | 73 | 66 | 75 | 36 | 37 | 29 | 12 | 4 | 8 | 448 |

From our experience and observations, we have come to feel that those who fall into the lower first and second deciles have a difficult time in carrying the university load in the School of Pharmacy. Those who fall in the third decile group can usually carry the work by considerable diligence and application. We have found that those who place themselves, by examination, in the fourth, fifth and upper decile groups can carry the work rather easily and oftentimes can do distinctive work, according to the standards set up by the University. While about twenty-six per cent of our students place themselves, according to these examinations, in the upper five decile groups, it is quite disappointing to know that the students who, by these examinations, display superior ability often do just enough to get by and do not distinguish themselves scholastically. This, of course, does not apply

to all of the students, but it is entirely too general as far as we are able to see, and is not confined alone to students in the School of Pharmacy.

Reference was made, early in this discussion, to the fact that we have a number of students who come and stay with us for a short time, drop out of the University and are never heard from again. In our files we find such notes as these: "Put on probation," "probation continued," "dropped by faculty action" and so forth. Beyond this we have not followed them.

It not infrequently happens that some of our students, who fell by the scholastic wayside, have gone out into business and are prosperous. This is all well and good, for perhaps such students were not happy in their college life and are much happier out doing something in the world of business. However, there is a possibility that some have left the University with disappointments and memories of failures that may mar their lives.

The University, however, tries all possible means to correct or alleviate any such stigma that might come upon the lives of these young men and women. This is not an easy thing to do in many cases.

TABLE II.

| Decile. | 1926. | | | 1927. | | | 1928. | | | 1929. | | | 1930. | | | 1931. | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | T.* | G.[1] | L.[2] | T. | G. | L. | T. | G. | L. | T. | G. | L. | T. | G. | L. | T. | G. | L. |
| 1– 10 | 4 | 3 | 1 | 2 | 0 | 2 | 8 | 3 | 5 | 5 | 0 | 5 | 3 | 0 | 3 | 4 | 1 | 3 |
| 11– 20 | 6 | 1 | 5 | 5 | 1 | 4 | 6 | 1 | 5 | 7 | 2 | 5 | 5 | 1 | 4 | 8 | 3 | 5 |
| 21– 30 | 15 | 6 | 9 | 7 | 0 | 7 | 10 | 3 | 5 | 4 | 3 | 1 | 3 | 1 | 2 | 4 | 0 | 4 |
| 31– 40 | 8 | 7 | 1 | 12 | 6 | 6 | 9 | 5 | 4 | 6 | 4 | 2 | 6 | 1 | 5 | 4 | 3 | 1 |
| 41– 50 | 6 | 1 | 5 | 8 | 3 | 5 | 9 | 8 | 1 | 3 | 1 | 2 | 3 | 0 | 3 | 5 | 2 | 3 |
| 51– 60 | 4 | 2 | 2 | 5 | 4 | 1 | 2 | 1 | 1 | 2 | 1 | 1 | 5 | 4 | 1 | 3 | 2 | 1 |
| 61– 70 | 9 | 5 | 4 | 3 | 2 | 1 | 3 | 1 | 2 | 3 | 3 | 0 | 5 | 2 | 3 | 2 | 1 | 1 |
| 71– 80 | 3 | 2 | 1 | 1 | 0 | 1 | 3 | 2 | 1 | 4 | 2 | 2 | 4 | 4 | 0 | 2 | 2 | 0 |
| 81– 90 | 1 | 1 | 0 | 3 | 1 | 2 | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 |
| 91–100 | 0 | 0 | 0 | 2 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 |
| Totals | 56 | 28 | 28 | 48 | 18 | 30 | 52 | 26 | 24 | 34 | 16 | 18 | 35 | 14 | 21 | 33 | 15 | 18 |

* T = Total.
[1] G = Graduated.
[2] L = Lost.

Table II is a summary of those students who entered the School of Pharmacy during the years 1926 to 1931, inclusive. All of those who entered during these years have either graduated or have left the University for other reasons. A glance at this table will indicate that we have at no time graduated more students than were lost from the school. In fact about 45% of those who entered were graduated. The remaining 55% left the University for various reasons. A majority of those entering before 1930 were enrolled in the three-year course.

It is a story that does not indicate very high educational efficiency, perhaps, but we hardly know just how badly we should feel about it. The thing that is disturbing is the fact that nearly 30% of the lowest ranking students have remained on and graduated while a number of the higher grade students have not graduated.

These facts are shown in Table III following, where the 258 students entering pharmacy from 1926 to 1931, inclusive, are listed by number and by percentages. As one might expect, the greatest losses are from the lower ranking groups.

TABLE III.

| | Decile Groups. | Students per Group. | Lost. Number. | Lost. Percentages. | Graduated. Number. | Graduated. Percentages. |
|---|---|---|---|---|---|---|
| 1 | 1– 10 | 26 | 21 | 70.08 | 7 | 29.92 |
| 2 | 11– 20 | 37 | 28 | 75.68 | 9 | 24.32 |
| 3 | 21– 30 | 43 | 30 | 69.77 | 13 | 30.23 |
| 4 | 31– 40 | 45 | 19 | 42.33 | 26 | 57.77 |
| 5 | 41– 50 | 34 | 19 | 55.89 | 15 | 44.11 |
| 6 | 51– 60 | 21 | 7 | 33.34 | 14 | 66.66 |
| 7 | 61– 70 | 25 | 9 | 44.00 | 14 | 56.00 |
| 8 | 71– 80 | 17 | 5 | 29.42 | 12 | 70.58 |
| 9 | 81– 90 | 6 | 2 | 33.34 | 4 | 66.66 |
| 10 | 91–100 | 4 | 1 | 25.00 | 3 | 75.00 |

We are not drawing conclusions from the study of these tables but the data present very serious educational and professional problems. First of all, there must be some reason or explanation for so many students dropping by the wayside before graduation time. We can explain this on the basis of the student's ability and various other factors that influence the lives of these young people, who come to us from homes over the state and country to enter into the life of the university and the college experience, but such explanations are inadequate. Some of them undoubtedly have backgrounds quite inadequate for such experiences as the college offers them, but this would not apply to all who fell by the wayside.

We are perhaps doing a very bad job of selecting the students who come to us. It would seem that we should know our students before they enter the University. From a knowledge of their experience, training and ability, we should be allowed to decide whether they are fully and thoroughly equipped to carry on the work expected of them in the School of Pharmacy and in other courses of the University.

As teachers of pharmacy we have a threefold obligation; namely, to the student, the state and the profession. We might fulfil these more efficiently and better by spending more time in selecting our students than in trying to salvage them.

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## TENTATIVE PROGRAM, THIRTY-SEVENTH ANNUAL MEETING OF THE AMERICAN ASSOCIATION OF COLLEGES OF PHARMACY, AUGUST 24–25, 1936.

### OFFICERS.

*President*, Robert C. Wilson; *Vice-President*, Homer C. Washburn; *Secretary-Treasurer*, Zada M. Cooper; *Chairman of the Executive Committee*, Charles B. Jordan.

### MONDAY, AUGUST 24TH.

9:00 A.M. Meeting of the Executive Committee.
9:30 A.M. Meeting of Teachers' Conference.

### CONFERENCE OF TEACHERS OF PHARMACY, AUGUST 24TH, 9:30 A.M.

*Chairman*, Emery T. Motley; *Vice-Chairman*, Robert C. Wilson; *Secretary*, Charles O. Lee.

### CONFERENCE OF TEACHERS OF CHEMISTRY, AUGUST 24TH, 9:30 A.M.

*Chairman*, Arthur H. Uhl; *Secretary*, Lewis C. Britt.

### CONFERENCE OF TEACHERS OF PHARMACOGNOSY AND PHARMACOLOGY, AUGUST 24, 1936.

*Chairman*, Charles E. F. Mollett; *Secretary*, Ralph D. Bienfang.

CONFERENCE OF TEACHERS OF PHARMACEUTICAL ECONOMICS, AUGUST 24, 1936.

*Chairman*, John F. McCloskey; *Secretary*, W. Henry Rivard.

SESSIONS OF THE ASSOCIATION.

FIRST SESSION, MONDAY, AUGUST 24th, 1:30 P.M.

Roll Call.
Appointment of Committee on Resolutions.
Address of the President, Robert C. Wilson.
Report of Secretary-Treasurer, Zada M. Cooper.
Report of Executive Committee, Charles B. Jordan.
Appointment of Nominating and Auditing Committees.
Reports of Standing Committees:
- Committee on Educational and Membership Standards, A. G. DuMez.
- Committee on Curriculum and Teaching Methods, L. Wait Rising.
- Committee on Activities of Students and Alumni, Edward J. Ireland.
- Delegates to the American Council on Education, Rufus A. Lyman.

Monday, August 24th, Annual Dinner, 6:00 P.M.

SECOND SESSION, MONDAY, AUGUST 24TH, 8:00 P.M.

Reports of Standing Committees (*Continued*):
- Committee on Relation of Boards and Colleges, C. Leonard O'Connell.
- Committee on Libraries, Charles O. Lee.
- Committee on Problems and Plans, Rufus A. Lyman.
- Syllabus Committee, J. G. Beard.

Reports of Special Committees:
- Committee on Student Branches of the AMERICAN PHARMACEUTICAL ASSOCIATION, William G. Crockett.
- Committee on the Establishment of a Pharmaceutical Corps in the United States Army, Edward Spease.
- Committee on Food and Drug Legislation, Charles B. Jordan.
- Committee on Pharmacy Aptitude Tests, Carl J. Klemme.

JOINT SESSION OF THE NATIONAL ASSOCIATION OF BOARDS OF PHARMACY AND THE AMERICAN ASSOCIATION OF COLLEGES OF PHARMACY, TUESDAY, AUGUST 25, 1936, 9:00 A.M.

Report of the Fairchild Scholarship Committee, E. G. Eberle.

THIRD SESSION, TUESDAY, AUGUST 25TH, 2:00 P.M.

Reports of Special Committees (*Continued*):
- Committee on Professional Relations, George C. Schicks.
- Committee on the Study of Examinations, C. Leonard O'Connell.

Reports of Special Representatives:
- Representative on American Council on Pharmaceutical Education, A. G. DuMez.
- Reporter on Biological Abstracts, Heber W. Youngken.
- Representatives to National Council on Pharmaceutical Research, Glenn L. Jenkins.
- Representatives to Druggists' Research Bureau, Paul C. Olsen.
- Representative to the National Association of Retail Druggists, Clair A. Dye.

Report of the Historian, Edward Kremmers.
Unfinished Business; Miscellaneous; Election of Officers; New Business; Executive Session.

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## TENTATIVE PROGRAM, NATIONAL ASSOCIATION BOARDS OF PHARMACY.

FIRST SESSION, MONDAY, AUGUST 24TH, 9:30 A.M.

1. Call to Order, President Mac Childs.
2. Roll Call.
3. Appointment of Committee on Credentials, President Mac Childs.

4. President's Address, Mac Childs.
5. Appointment Committee on President's Address.
6. Report of Secretary, H. C. Christensen.
7. Report of Treasurer, J. W. Gayle.
8. Appointment of Nominating Committee, President Childs.
9. Report of Executive Committee, Clare Allan, *Chairman*.
10. Presentation of Suggested Amendments to Constitution and By-Laws, Walter Varnum.

SECOND SESSION, MONDAY, AUGUST 24TH, 1:30 P.M.

1. Report of Advisory Examination Committee, H. C. Christensen, *Chairman*.
2. Report of Syllabus Committee.
3. Report of Legislation Committee, G. A. Moulton, *Chairman*.
4. Report of Committee on National Legislation, Robert L. Swain, *Chairman*.
5. Report of Committee on Prerequisite Legislation, C. W. King, *Chairman*.
6. Report of Publicity Committee, Hugh P. Beirne, *Chairman*.
7. Report of Grievance Committee, M. N. Ford, *Chairman*.
8. Report of Committee on National Certificate, H. C. Christensen, *Chairman*.
9. Report of Committee on Minimum Standards of Technical Equipment, A. C. Taylor, *Chairman*.
10. Report of Committee on Pharmaceutical Jurisprudence, Roy B. Cook, *Chairman*.
11. Report of Committee on Code Matters, Robert L. Swain, *Chairman*.
12. Report of Banquet Committee, Walter H. Cousins, *Chairman*.

N. A. B. P. Banquet, Monday, August 24th, 6:30 P.M.

JOINT SESSION WITH AMERICAN ASSOCIATION COLLEGES OF PHARMACY, TUESDAY, AUGUST 25TH, 9:00 A.M.

FINAL SESSION, TUESDAY, AUGUST 25TH, 1:30 P.M.

1. Reports of Vice-Presidents.

   District No. 1, V.-P. George A. Moulton.
   District No. 2, V.-P. J. M. Woodside.
   District No. 4, V.-P. Earl Durham.
   District No. 6, V.-P. Emmett Weaver.
   District No. 7, V.-P. R. C. Shultz.

2. Report of Committee on President's Address.
3. Report of Department of Education, R. L. Swain, *Director*.
4. Report of Committee on Constitution and By-Laws, Walter Varnum, *Chairman*.
5. Report of Resolutions Committee, A. C. Taylor, *Chairman*.
6. Reports of Special Committees.
7. Unfinished Business.
8. New Business.
9. Report of Nominating Committee.
10. Election and Installation of Officers.
11. Adjournment.

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## PROGRAM OF NATIONAL CONFERENCE ON PHARMACEUTICAL RESEARCH, 1936 MEETING, DALLAS, TEXAS, AUGUST 22, HOTEL ADOLPHUS.

FIRST SESSION, 2:00 P.M.

1. Call to Order by Chairman.
2. Appointment of Nominating Committee.
3. Summary of Year's Activities and Outlook of Conference for the Future, by Chairman Gathercoal.
4. Reports of Officers.
   *a*. Report of Secretary.

*b.* Report of Treasurer.
*c.* Report of Executive Committee by Secretary.

5. Reports of Standing Committees.
   (1) Physical Chemistry, Arthur Osol, *Chairman.*
   (2) Bacteriology and Immunology, Louis Gershenfeld, *Chairman.*
   (3) Pharmacognosy, Heber W. Youngken, *Chairman.*
   (4) Pharmacology and Bioassays, James C. Munch, *Chairman.*
6. Roll Call of Delegates.
7. Adjournment for Dinner. Arrangements Will Be Made for a Dinner for the Delegates Assembled.

An address pertinent to the work of the Conference will be delivered.

EVENING SESSION, 8:00 P.M.

8. (5) Medicinal Chemicals, Joseph Rosin, *Chairman.*
   (6) Endocrinology, Arthur Grollman, *Chairman.*
   (7) Manufacturing Pharmacy, L. Wait Rising, *Chairman.*
   (8) Pharmaceutical Dispensing, William J. Husa, *Chairman.*
   (9) Educational Methods, A. B. Lemon, *Chairman.*
   (10) Pharmaceutical Economics, Harry S. Noel, *Chairman.*
   (11) Historical Pharmacy, Charles H. LaWall, *Chairman.*
9. Reports of Other Special Committees.
   (1) Publications, Edward N. Gathercoal, *Chairman.*
   (2) Census of Research, James C. Munch, *Chairman.*
10. General Discussion of the Status of Pharmaceutical Research.
11. Election and Installation of Officers.
12. Adjournment.

*Chairman*, E. N. Gathercoal; *Secretary*, John C. Krantz, Jr.

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## CORRECTIONS IN THE U. S. P. XI.

Since the appearance of the new Pharmacopœia in December of 1935, the text has been subjected to intensive review and some corrections have been found necessary. In so far as these cover typographical errors or accidental inaccuracies, authority has been given to publish the list of corrections in pharmaceutical and medical journals.

Purchasers of the new Pharmacopœia may also obtain a printed list of these corrections for insertion in their copies of the U. S. P. Send a 3-cent stamp to the publishers of the Pharmacopœia, the Mack Printing Company, Easton, Pa.

Questions have also arisen concerning certain Pharmacopœial assays or tests and these are under investigation. In those cases where it becomes desirable to revise any of the printed monographs such changes will be announced by "Interim Revision" procedure.

### NATURAL WATER VERSUS DISTILLED WATER IN DRUG EXTRACTION, ETC.

The new Pharmacopœia directs that distilled water shall be used in all formulas, but a further study of the difficulties involved has led the Committee to revise this requirement and permit the use of a *natural water* of good quality as an alternative to distilled water in the extraction of U. S. P. vegetable drugs and in the manufacture of Resin of Podophyllum and of Saponated Solution of Cresol. This is of the nature of an "interim revision" and a formal statement permitting the alternative use of natural water and establishing standards for it will be issued in the near future as an Interim Revision.

In addition to this revision of the distilled water requirement, other interim revision changes will soon be announced.

E. FULLERTON COOK, *Chairman.*

*Corrections in N. F. VI will be found at end of Council Letter No. 21, this issue of the* JOURNAL.

## CORRECTIONS IN THE UNITED STATES PHARMACOPŒIA, ELEVENTH REVISION.*

To be made in copies numbers 100,001 to 150,000.

| Page. | Lines. | |
|---|---|---|
| lxx | | Under "Hydrastis" and the sub-head "Pulvis Hydrastidis" *change* "Hydrastis" *to* "Hydrastine". |
| lxxiv | | *Change* "Theophyllina cum Sodii Acetas" *to* "Theophyllina cum Sodii Acetate." |
| 19 | 4–6 | *Change to:* "Mix 0.5 Gm. of powdered Citric Acid with 5 cc. of sulfuric acid in a test-tube that has been previously rinsed with sulfuric acid and maintain the temperature of the mixture at 90° C. for one hour: the color of the mixture is not darker than matching fluid K, described under the test for *carbonizable substances*, page 441." |
| 32 | 1–3 | *Change to:* "The potency of Aconite shall be such that 0.1 Gm. of it, when extracted and assayed as directed under *Tinctura Aconiti*, page 391, shall possess an activity equivalent to not less than 0.150 milligram of reference aconitine." |
| 32 | | Fifth line from bottom of page: *Change* 14.3 *to* 15.8. |
| 78 | 1–4 | *Change to:* "The solution produced by dissolving 0.2 Gm. of Atropine Sulfate in 5 cc. of sulfuric acid has no more color than matching fluid A, described under the test for *carbonizable substances*, page 441, and the solution becomes only light yellow upon the addition of 0.2 cc. of nitric acid (*many other alkaloids*)." |
| 96 | 33–46 | *Change to:* "*Assay:* Weigh accurately in a glass-stoppered weighing tube about 0.4 Gm. of Calcium Bromide, dissolve it in 100 cc. of distilled water and add 1 cc. of hydrochloric acid. Heat the solution to boiling and add, with stirring, an excess of hot ammonium oxalate T.S., then make slightly alkaline with ammonia T.S. Heat the mixture on the water-bath for two hours, filter through hardened filter paper and wash thoroughly with warm distilled water. Puncture the filter paper, wash the precipitate into a beaker by means of a stream of hot distilled water, followed by 30 cc. of dilute sulfuric acid (1 in 3), heat the solution, if necessary, to 60° C. and titrate with tenth-normal potassium permanganate. Each cc. of tenth-normal potassium permanganate is equivalent to 0.009996 Gm. of $CaBr_2$." |
| 97 | 43 | *Change* 0.05004 Gm. *to* 0.005004 Gm. |
| 103 | 18 | *Change to:* "The specific rotation $[\alpha]_D$ of Natural Camphor, determined at 25° C., in a solution containing 10 Gm. of Camphor in sufficient alcohol to make 100 cc. and using a 200-mm. tube, is between +41° and +42°, page 459." Omit all reference to the specific rotation of Synthetic Camphor. |
| 118 | 12 | *Change* 0.5 Gm. *to* 0.2 Gm. |
| 125 | | Third line from bottom of page: *Change* 0.5 Gm. *to* 0.01 Gm. |
| 126 | 10 | *Change* 433.25 to 424.24. |
| 127 | 32 | *Change* "0 45" *to* 0.45. |
| 135 | 21–22 | *Add* between the lines: "NOTE: In preparing aqueous solutions of Dextrose it is permissible to use a dextrose which does not conform to the official requirements for |

* A copy of this list may be obtained by a purchaser of the U. S. P. XI by sending a 3-cent stamp, to cover postage expense, to the publishers of the Pharmacopœia, the Mack Printing Company, Easton, Pa.

water of hydration, provided the product meets all other official tests for purity and also provided suitable allowance is made for the difference in water content."

139 17 *Change* 0.5 Gm. *to* 0.1 Gm.
150 12 *Change* 0.3 Gm. *to* 0.03 Gm.
150 12 *Change* 5 grains *to* 1/2 grain.

180 11–14 *Change to:*

"Vigorously shake 5 cc. of Glycerin with 5 cc. of sulfuric acid in a glass-stoppered 25-cc. cylinder for one minute and allow the liquid to stand for one hour; it does not become darker than 10 cc. of matching fluid H, described under the test for *carbonizable substances*, page 441."

195 Fourth line from bottom of page: *Change* 62 *to* 63.
195 Fifth line from bottom of page: *Change* 61 *to* 60.
196 29–30 *Change* "continue the heating" *to* "maintain the crucibles and mass at dull redness."
208 33 Add the synonym "Viosterol in Oil."
208 44 *Delete:* "Unsaponifiable matter: not more than 2 per cent, page 446."
231 Fourth line from bottom of page, *delete:* "natural."
231 Fifth line from bottom of page, *change* 42° and 44° C. *to* 41° and 43° C.
235 Fourth line from bottom of page, *change* 0.2 Gm. *to* 0.12 Gm.

278 21 *Insert* before "Add:"

"Place 100 cc. of distilled water in a 300-cc. Erlenmeyer flask, add 5 cc. of Paraldehyde, and shake the mixture gently until solution is complete."

289 Sixth line from bottom of page, *change* 0.5 Gm. *to* 0.1 Gm.
290 Twelfth line from bottom of page, *change* 0.5 Gm. *to* 0.1 Gm.
313 6 *Change* 0.5 Gm. *to* 0.2 Gm.
313 Last line at bottom of page, *change* 0.5 Gm. *to* 0.2 Gm.
315 27 *Change* 0.5 Gm. *to* 0.2 Gm.
316 14 *Change* 0.5 Gm. *to* 0.2 Gm.
317 17 *Change* 0.5 Gm. *to* 0.2 Gm.
318 22 *Change* 0.5 Gm. *to* 0.2 Gm.
319 8 *Insert* after "444:" "using about 1 Gm. of the Rosin accurately weighed."
321 5 *Delete* "or" and *insert* after "species:" "(except *Rheum rhaponticum*) or of."
322 22 *Change* 0.5 Gm. *to* 0.2 Gm.
324 Line 10 from bottom of page, *change* 0.5 Gm. *to* 0.1 Gm.
353 30 *Change* 25 cc. *to* 5 cc.
353 39 *Change* 25 cc. *to* 5 cc.
362 Ninth line from bottom of page, *change* 0.5 Gm. *to* 0.1 Gm.
363 30 *Change* 0.5 Gm. *to* 0.2 Gm.
368 31 *Change* 7.243 *to* 7.281.
377 *Insert* between the third and fourth line from bottom of page: "*Alcohol content*—From 1 to 2 per cent, by volume, of $C_2H_5OH$."
378 27 *Change* 7.5 to 8.5 *to* 8.5 to 11.
383 5 *Change* 0.5 Gm. *to* 0.2 Gm.
384 20 *Change* 0.5 Gm. *to* 0.2 Gm.
384 33 *Change* 70 *to* 75.
384 34 *Change* 80 *to* 85.
391 25–32 *Change* the directions to:

"Prepare a tincture by Process P, as modified for assayed tinctures, page 390, using a mixture of 3 volumes of alcohol and 1 volume of distilled water as the menstruum. Macerate the drug during twenty-four hours and then percolate it at a moderate rate. Immediately add sufficient hydrochloric acid to this percolate to produce a $p_H$ of 3 ± 0.2, page 576. Assay

| | | |
|---|---|---|
| | | a portion of the percolate and adjust the volume of the remaining liquid by dilution with the above menstruum, including sufficient hydrochloric acid to produce a $p_H$ of 3 ± 0.2, page 576, so that the finished Tincture will conform to the above biological standard." |
| 399 | | *Insert* between the tenth and eleventh lines from the bottom of page: "*Alcohol content*—From 58 to 64 per cent, by volume, of $C_2H_5OH$." |
| 488 | 28 | *Change* 0.1631 Gm. *to* 0.1814 Gm. |
| 572 | 25 | *Change* 0.02041 *to* 0.2041. |
| 592 | 14 | *Change* 433.25 *to* 424.24. |

## SUGGESTED MOUTH WASH PRESCRIPTIONS FOR USE IN DENTAL PRACTICE.*

The Committee desires to exchange publicity material distributed to the medical profession.

℞

| | Apoth. Metric. |
|---|---|
| Liq. Antisept. N. F. | f℥ viii 240 cc. |

Sig: Dilute with equal parts of water as a mouth wash.

NOTE: This same preparation may be prescribed by writing the official Latin title—*Liquor Antisepticus N. F.* or the official English title—*N. F. Antiseptic Solution.*

Another way of writing the same prescription.

℞

| | |
|---|---|
| Liq. Antisept. N. F. | f℥ iv 120 cc. |
| Aq. Dest. | qs. f℥ viii 240 cc. |

M.

Sig: Use undiluted as a mouth wash.

NOTE: To color the above prescription red add

| | |
|---|---|
| Liq. Amaranth. N. F. | *m* x 0.6 cc. |

℞

| | |
|---|---|
| Liq. Arom. Alk. | f℥ viii 240 cc. |

Sig: Use undiluted as a mouth wash.

NOTE: For use in *dental spray bottle* dilute with 5 volumes of water.

Official Latin title—*Liquor Aromaticus Alkalinus*, Official English title—*Alkaline Aromatic Solution.*

This preparation is red in color.

℞

| | Apoth. Metric. |
|---|---|
| Liq. Iodi Phenol. | f℥ viii 240 cc. |

Sig: Dilute with equal parts of water as a mouth wash.

NOTE: This same preparation may be prescribed by writing the official Latin title—*Liquor Iodi Phenolatus*, or the official English Title—*Phenolated Solution of Iodine*, or the official synonyms—*Boulton's Solution, French Mixture* or *Carbolized Solution of Iodine.*

Another way of writing the same prescription.

℞

| | |
|---|---|
| Liq. Iodi Phenol. | |
| Aq. Dest. | aa f℥ iv 120 cc. |

M.

Sig: Use undiluted with water.

℞

| | |
|---|---|
| Liq. Sod. Bor. Co. | f℥ viii 240 cc. |

Sig: Use as a mouth wash.

NOTE: The official Latin title for this preparation is—*Liquor Sodii Boratis Compositus*, Official English title—*Compound Solution of Sodium Borate*, official synonym—*Dobell's Solution.* (*To be continued.*)

* U. S. P.-N. F. Publicity Committees of the Maryland State Dental Association, Maryland Pharmaceutical Association and Baltimore Retail Druggists' Association.

## TEXAS WILD FLOWERS.

This profusion of wild flowers on Texas roadsides is not accidental. It results from planned efforts of the State Highway Department in roadside improvement. In all parts of the State, highway maintenance men mow flowers that have gone to seed. They cut not only along the roads but also—with the owners' permission—in farmers' fields in which desirable wild flowers are abundant.

# PROCEEDINGS OF THE LOCAL BRANCHES

"All papers presented to the Association and Branches shall become the property of the Association with the understanding that they are not to be published in any other publication prior to their publication in those of the Association, except with the consent of the Council." —Part of Chapter VI, Article VI of the By-Laws.

ARTICLE III of Chapter VII reads: "The objects and aims of local branches of this Association shall be the same as set forth in ARTICLE I of the Constitution of this body, *and the acts of local branches shall in no way commit or bind this Association, and can only serve as recommendations to it.* And no local branch shall enact any article of Constitution or By-Law to conflict with the Constitution or By-Laws of this Association."

ARTICLE IV of Chapter VII reads: "Each local branch having not less than 50 dues-paid members of the Association, holding not less than six meetings annually with an attendance of not less than 9 members at each meeting, and the proceedings of which shall have been submitted to the JOURNAL for publication, may elect one representative to the House of Delegates."

Reports of the meeting of the Local Branches shall be mailed to the Editor on the day following the meeting, if possible. Minutes should be typewritten with wide spaces between the lines. Care should be taken to give proper names correctly and manuscript should be signed by the reporter. *Please advise us of changes in Roster and mail reports promptly.*

## CHICAGO.

The monthly meeting of the Chicago Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held Tuesday evening, April 21st. This was the last meeting of the Branch until the beginning of school in the Fall. Over one hundred members and their friends were present at the meeting which ended a very successful term of monthly meetings from the standpoint of speakers presented and attendance.

President Morrison opened the meeting with a brief summary of the activities of the Branch during the past school year.

Secretary Templeton presented a short financial report which showed the Branch in a very favorable financial condition as compared with recent years. Nineteen new members have been secured since September 1935.

Mention was made of the Convention to be held at Dallas, Texas, August 24th–29th and that many members from the Chicago territory are planning to attend.

President Morrison introduced the speaker of the evening, Dr. Hutton, past-president of the Chicago Medical Society and eminent physician. Dr. Hutton spoke on the subject of "Practical Endocrinology."

Dr. Hutton listed the hormones of the Anterior Pituitary as growth hormone, sex hormone, adrenotropic, thyrotropic, parathyrotropic, lactogenic and diabetogenic. The parathyrotropic hormone has been discussed but not agreed upon as to actual existence. The diabetogenic hormone has to do with fat and carbohydrate metabolism.

For a long time physicians have known that mothers afflicted with pituitary deficiency have been unable to nurse their babies and with present knowledge this is attributed to a deficiency of the lactogenic hormone.

In many cases where the sex hormone is over-functioning the growth hormone is found to be in deficiency and vice versa.

Names of some of the preparations of the anterior lobe of the pituitary gland were mentioned as Thyrotropic, Andrenotropic, Prolactin, Polyansyn and Antuitrin.

Slides were shown depicting pituitary deficiency and, incidentally, it was mentioned by Dr. Hutton that measles is sometimes followed by a lack of pituitary secretion.

Preparations of the growth hormone of the pituitary were mentioned as Antuitrin G and Phyone. The sex hormone (also known as maturity or gonadotropic hormone) preparations were listed as Antuitrin S, Follutein, A. P. L., and Prephysin. The Antuitrin S and Follutein are obtained from pregnancy urine.

Sources of the gonadotropic principles are: Anterior lobe of the pituitary gland, pregnancy urine and blood, menopause urine, castrate urine and placenta.

The gonadotropic principles are effective only where the ovaries are present while the estrogenic principles are effective when the gonads are absent.

Posterior Lobe preparations mentioned were: Pitressin, Pitocin and Pituitrin. Slides were shown of the effect of malfunction of the fat metabolism hormone present in the posterior lobe.

Estrogenic preparations mentioned were Amniotin, Theelin, Theelol, Progynon, Sistomensin, Agomensin, Progestin, Emmenin, Ovarian Substance and Ovarian Residue.

The ovary owes its impetus to growth to the anterior pituitary and later the ovary exerts an inhibitory action on the pituitary. Many times there is too fine a discrimination for the clinician, so then the whole gland should be used. These glandular disturbances are hereditary or caused by disease and there is need for long and thorough treatment with an understanding by the patient that results probably will not be immediate or may be negative.

Persons with pituitary disturbances are prone to severe headaches and this symptom is a guide in many cases to the physician.

The testicular hormone has been investigated and there is a question as to whether one or two hormones exist. Preparations of the testicular hormone were mentioned as Androsterone (from the testicle), Androsterone (synthetic), Testosterone, Androstine and Stanley's Material.

Tumors of the pineal gland give rise to excessive genital growth.

Hypertension and Diabetes are sometimes relieved by small doses of X-ray to the pituitary and adrenal glands.

Dr. Hutton ran a constant series of slides throughout his lecture that were very informative and gave a clear picture of the physical deformatives caused by malfunction of the gland under discussion.

Questions were asked by members of the group and the meeting was closed by a standing expression of thanks to Dr. Hutton for his very clear discussion.

L. TEMPLETON, *Secretary.*

## NEW YORK.

The regular meeting of the New York Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held on Monday evening, April 13, 1936, at Columbia University, College of Pharmacy.

The meeting was called to order at 8:30 P.M., President Schaefer presiding. The minutes of the March meeting were read and approved.

Chairman Hauck, of the Committee on Membership, submitted the application for membership in the Branch of Raymond F. James; he was elected to membership.

Chairman Lehman, of the Committee on Education and Legislation, reported as follows:

*Federal Legislations.*—Robinson-Patman Bill: H. R. 8442, with amendments was reported to the House Judiciary Committee on March 31st. The amendment provides that "nothing in this bill shall prevent a coöperative association from returning to its members or a coöperative wholesale association from returning to its constituent retailer members—net earnings in proportion to their sales to, from and through such associations."

It is expected that the Copeland Bill S. 5 will be reported to the House Interstate & Foreign Commerce Committee. This is the new law to control the Food, Drug and Cosmetic industry, and is to supplant the present Pure Food and Drugs Act. It is hoped that its passage may be insured.

The Doughton Act, H. R. 11452, placing the control of the Secret Service Division, a Liquor Enforcement Section, a Counterfeiting Section, a Customs Section, a Section on Personnel and a Section on Narcotics, is now lying dormant, but renewed efforts are being made to secure its enactment, in spite of the opposition to the measure from influential sources. A joint committee composed of the representatives of the AMERICAN PHARMACEUTICAL ASSOCIATION, the Federal Wholesale Druggists Association, the American Drug Manufacturers Association and Admiral R. P. Hobson of the World Narcotic Educational Association are drafting an amendment perpetuating the Bureau of Narcotics as a separate establishment of the Treasury Department.

*State Legislation.*—Twomey-Averill Bill. To amend the education law in relation to the definition of Chemist used in Article 51, has been reported out favorably.

Twomey-Averill bill to amend the education law in relation to the revocation of license to practice pharmacy, has been reported out favorably.

Dunckel-Milmoe bill which forbids the sale at wholesale of Poisonous, Habit-forming or Deleterious drugs to unlicensed dealers, has been killed in committee.

Twomey-Piper bill designed to limit the opening of new pharmacies and drug stores, has been killed in committee.

Senate 849, print 930, Feld, Assembly 1408, print 1567, Piper. This is a stop-loss provision measure, which forbids the sale of any drug store merchandise at a price below the manufacturer's list price per dozen, and its enforcement is confined to the retail drug business entirely. This bill has been favorably reported out of committee, and seems to have a good prospect of being passed.

The Livingston New York State Distributive Trades Commission Act, Senate 1355, print 1578, is being well received in many groups, provides for a formation of a commission, similar to the Federal Trade Commission, which will have control of the distribution of merchandise and which is to prevent unfair competition, etc. This provides for commissioners and a bureau, the funds for the support of which will be provided by taxation: proportionately to the income of each establishment. Efforts are being made to put this law through, but it may have to lay over till next session.

Mr. Schaefer reporting as a delegate to the New York Pharmaceutical Council said that the election of officers would take place on the first day of the N. Y. All City Fair Trade Convention and that it was necessary to increase the number of delegates to the full number permitted. He, therefore, announced that he had appointed the following as delegates:

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|---|---|---|---|
| *Delegates:* | F. C. A. Schaefer | *Alternates:* | John J. Corcoran |
| | Samuel C. Henry | | George Christ |
| | Jacob Seley | | Milton S. Malakoff |
| | H. H. Blomeier | | Dr. F. A. Leslie |
| | Chas. Heimerzheim | | George Decker |
| | Dr. Geo. C. Diekman | | |

and requested the approval of the Branch for his action:

Dr. Hugo Schaefer moved that the action of the president be endorsed. Motion seconded by Dr. Wimmer; carried.

Dr. Wimmer moved that the Branch instruct the delegates to cast their vote in support of the ticket presented in the report of the nominating committee. This was seconded by Mr. Lehman, and carried.

The secretary was instructed to write to the delegates and inform them of their instructions.

Secretary Schaefer, of the Remington Medal Committee, reported that Dr. Edmund N. Gathercoal will be the recipient of the Honor medal for 1936. He moved that the secretary write Dr. Gathercoal, congratulating him upon the honor and asking his pleasure with regard to the presentation. Dr. Wimmer seconded and the motion was carried.

As delegate to the House of Delegates, Dr. Schaefer stated that as it was customary for the convention of the AMERICAN PHARMACEUTICAL ASSOCIATION to go to a different section of the country each year, it should return to the East in 1937. He suggested that a committee be appointed to study the question as to whether or not it would be feasible to invite the convention to come to New York at that time. Dr. Wimmer moved that Dr. Schaefer be appointed to act for the Branch. Motion was seconded and carried.

Chairman Steiger, of the Committee on the Progress of Pharmacy, reported as follows:

"A patent assigned to Chemische Fabrik. Sandoz describes the separation of Ergot alkaloids by chromatographic absorption according to the method of Tawett. The crude extracts of the alkaloids are dissolved in indifferent solvents such as benzene or its homologs, and the solutions are passed into a column containing absorbents insoluble in the solvents used, *e. g.*, sugar, lime, etc. By diffusion of the solution in the absorbent column there appears a chromatogram visible to ultraviolet light. Examples are given of the separation of ergotamine and ergotaminine, ergotoxin and ergotinine (*C. A.*, Vol. 30, No. 6)."

The *Chemist & Druggist* (London 2/15/36) comments on an article on "Oral Vaccine for Colds" in *The British Medical Journal*. Five strains of Pfeiffer's bacillus along with a strain of A. bronchitica are grown together in bacterial symbiosis, in blood agar broth flasks for seven days. The culture is killed with 1% phenol over night. It is then diluted with an equal amount of sterile saline so as to reduce the phenol content to $^1/_2$% and tested for sterility. By a process of trial and error the optimal dose was determined. The results obtained since September are

distinctly encouraging, indicating that specific agglutins to Pfeiffer's bacillus are formed, and that antitoxins appear in the blood after oral administration of the broth culture described.

*Drug Trade News* (3/16/36) tells of a patent assigned to Winthrop Chemical Co., for Vitamin D solutions in glycols. These higher glycol derivatives permit Vitamin D to be administered to infants in water-soluble form.

President Schaefer called for a discussion on ways to increase attendance at regular meetings. After considerable discussion it was moved that a committee be appointed to investigate the subject. The motion was seconded and carried.

President Schaefer then introduced the guest speaker, Prof. George C. Schicks, who addressed the Branch on the subject of "The Challenge of Dentistry to Scientific Pharmacy."

The speaker stated that a real challenge existed in the relations between dentists and pharmacists. The dentists are an enthusiastic group with which to work. They are willing to listen and to learn what the pharmacist has to teach. The dentist does not know of the U. S. P. and N. F. preparations which he can obtain from the pharmacist and it is the pharmacist's job to give him the information. The dentist, perhaps without even knowing it, needs the professional services of the pharmacist.

If the pharmacists will prepare correctly the official preparation which may be used by the dentist, and will detail the dentist with these preparations, they will be amply rewarded for their trouble. The dentist will pay good prices for what he gets. He is used to it.

The speaker distributed a pamphlet of "Dental Prescriptions for Office and Patient's Use." This contained a number of official and unofficial preparations of proved value.

After considerable discussion, a rising vote of thanks was accorded the speaker and the meeting adjourned.

HORACE T. F. GIVENS, *Secretary.*

## PHILADELPHIA.

The April meeting of the Philadelphia Branch, AMERICAN PHARMACEUTICAL ASSOCIATION, was called to order at 8:15 P.M., April 15th, at the Philadelphia College of Pharmacy and Science, by President Lawrence L. Miller.

The minutes of the March meeting were read and approved.

Dr. James C. Munch, of the membership committee, presented the following applications for membership in the local branch: Martin Ulan, Wilton Kimmer, Albert Chiola, Nathan Zonies, Dr. Thomas M. Logan, Prof. Neal Bowman. The applicants were duly elected to membership and the secretary was instructed to place their names on the official files upon presentation of the usual fee of one dollar.

President Miller announced the following committees to serve for the year 1936–1937:

*Program Chairman*, James C. Munch, Frank H. Eby, E. H. MacLaughlin, Alfred Barol, H. Evert Kendig.

*Membership Chairman*, S. H. Kerlin, Frank Law, James C. Munch, E. H. MacLaughlin, N. A. Simpson, Harry M. Mantz, Elwood S. Paisley.

*Professional Relations Chairman*, W. A. Pearson, H. Evert Kendig, Wilmer Krusen.

*Entertainment Chairman*, Adley B. Nichols, Marin S. Dunn, Arthur K. Leberknight.

*Practical Pharmacy Chairman*, Ambrose Hunsberger, E. T. Hahn, Theodore Campbell, Jr.

It was a pleasure to have two guest speakers on this occasion: J. Leon Lascoff, *First Vice-President* (elect) of the AMERICAN PHARMACEUTICAL ASSOCIATION, member of the New York Board of Pharmacy and an outstanding retail pharmacist spoke on, "Problems in Pharmacy, and How to Solve Them." J. B. Pilchard, Secretary of the Pennsylvania Pharmaceutical Association, and an ardent worker in pharmaceutical circles spoke on "Looking Ahead in Pharmacy."

These eminent speakers made this meeting one of the outstanding meetings of the Branch. Dr. Lascoff tabulated and spoke on nine of the major problems that face the retail pharmacist. These problems were well planned and thoroughly discussed and analyzed. Dr. Lascoff presented some twenty prescriptions that frequently trouble the compounding pharmacist. He spoke on and illustrated the right and the wrong way to compound these prescriptions. The members of the Branch were pleased with the masterful way in which Dr. Lascoff handled these difficult incompatibilities. Many questions were asked by the membership.

Secretary Pilchard emphasized and evaluated the need of organization in the profession.

The local branch is in accord with Mr. Pilchard's remark that "complete organization is one method of solving many of our problems." As he stated, "Our aim is to get those pharmacists who do not attend to attend, for we who do attend, already realize the need, hence we are here." Mr. Pilchard spoke of the value of the pharmacist and the Pennsylvania Pharmaceutical Association in those sections of Pennsylvania which were inundated during the floods.

A rising vote of thanks was given the speakers for their excellent presentations.

GEORGE E. BYERS, *Secretary.*

MAY.

The May meeting of the Philadelphia Branch, AMERICAN PHARMACEUTICAL ASSOCIATION, was held at Sharp and Dohme Laboratories, Glen Olden, Penna., Tuesday night, May 12, 1936. The meeting was called to order by President L. L. Miller. The reading of the minutes was dispensed with.

The Branch was favored by two excellent speakers: Dr. J. E. Schneider of Sharp and Dohme presented a most learned dissertation on "Rabies." Dr. Thomas S. Githens, also of Sharp and Dohme, presented the ever-popular "Snakes and Antivenin."

Dr. Schneider pointed out that if an individual was bitten by a dog, the animal should immediately be placed in quarantine, under competent supervisors, and the individual be given Rabies treatment at once. If at the end of seven days the animal is found to be not rabid, he could be released and the person's treatments could be discontinued. He stated that seasons had little to do with the prevalence of the infection. He discussed in detail the preparation of Rabies Vaccine and its use. This pertinent subject brought forth many interesting questions from the group.

Dr. Githens' subject, as always, was well presented and again the interest and fascination in snakes was demonstrated by the variety of questions it called forth. The audience was pleased with the demonstration of the value of Antivenin. Dr. Githens injected two pigeons; one with venom and the other with venom and antivenin; in a very short time the results were in evidence. The movie on how snake venom is collected was well received. Of unusual interest was the demonstration of "The Black Widow" Spider. The hearers were glad to learn that science has succeeded in securing therapeutic treatment against this deadly bite.

A rising vote of thanks was given the speakers for their coöperation in making this meeting a success.

Chairman Kerlin, of the Membership Committee, presented the following applications for the Local Branch: Robert Reubush, Paul B. Robinson, Frederich Scholl.

Applications for the Parent Body: J. W. Jester, Sr., David Phillips.

The applicants were elected to membership in the Local Branch.

The business meeting was preceded by a dinner at Sharp and Dohme's. This was attended by forty-two guests.

GEORGE E. BYERS, *Secretary.*

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## REPORT OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION ON THE NEW ERGOT ALKALOID.

The Council of Pharmacy and Chemistry of the American Medical Association has made the following report on the new ergot alkaloid:

During the past year, communications from four laboratories have been published reporting the isolation of a new oxytocic alkaloid from ergot. Until recently there has been doubt as to whether or not the principles reported by these laboratories were identical (termed "Ergotocin" by Kharasch, "Ergometrine" by Dudley and Moir, "Ergobasine" by Stoll and "Ergostetrine" by Thompson). In a jointly signed statement (*Science*, February 28th) Kharasch, King (acting for Dudley), Stoll and Thompson say there is "no doubt that the alkaloid obtained in the four different laboratories was the same substance. . . ."—*Science*, March 27, 1936.

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# ASSOCIATION BUSINESS

## AD INTERIM BUSINESS OF THE COUNCIL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, 1935–1936.

Office of the Secretary, 2215 Constitution Ave., Washington, D. C.

LETTER NO. 19.

April 25, 1936.

*To the Members of the Council:*

*119. Use of Text of N. F. VI.* Motion No. 52 (Council Letter No. 18, page 366) has been carried and Dr. Blayney has been so advised.

P. Blackiston's Son & Co., Inc., Philadelphia, Pa., have requested permission to use the text of N. F. VI for partial reproduction in the following books: Gould, "New Medical Dictionary," 4th Edition (Reprint); Gould, "Pocket Pronouncing Medical Dictionary," 10th Edition (Reprint); Scoville, "The Art of Compounding," 6th Edition; Youngken, "A Textbook of Pharmacognosy," 4th Edition.

Chairman DuMez of the Committee on Publications recommends that the request be granted under the usual conditions and at the usual fee of $5.00 in each case.

(*Motion No. 55*) It is moved by DuMez that P. Blackiston's Son & Co., Inc., be granted permission to use portions of the text of the N. F. VI in Gould. "New Medical Dictionary," 4th Edition; in Gould, "Pocket Pronouncing Medical Dictionary," 10th Edition; in Scoville, "The Art of Compounding," 6th Edition; and in Youngken, "A Textbook of Pharmacognosy," 4th Edition, with the customary acknowledgment and at the usual fee of $5.00 in each case.

The following letter has been received from Professor E. Fullerton Cook (see Council Letters Nos. 16, page 364 and 17, page 365):

> "In a letter dated December 24, 1935, I requested permission to use certain portions of the N. F. VI text in the forthcoming edition of 'Remington's Practice of Pharmacy.' Evidently this was granted as a bill was recently received covering the charge.
>
> "In further studying the situation it has been decided that it will be necessary to change the first plan and use the text very much as in the Seventh Edition. In other words we find it possible, at least in some instances, to use chemical tests and assays and prefer to have permission to use the official wording rather than to rewrite it.
>
> "I would therefore respectfully request, in the name of the Publishers, J. B. Lippincott Company, permission to use such portions of the N. F. VI as may be desirable following the same style as was used for the Seventh Edition of the 'Remington.' $1000.00 was charged for this privilege ten years ago."

Chairman DuMez of the Committee on Publications recommends that permission be granted under the conditions set forth in Professor Cook's letter.

(*Motion No. 56*) It is moved by DuMez that permission be granted to E. Fullerton Cook, for the J. B. Lippincott Co., to use portions of the text of the N. F. VI in a new edition of "Remington's Practice of Pharmacy" to the extent used in the Seventh Edition, with the usual acknowledgment and at the same charge of $1000.00.

*120. University of Mississippi Student Branch.* Motion No. 53 (Council Letter No. 18, page 366) has been carried and the application and the Constitution of the Branch are approved.

*121. Election of Members.* Motion No. 54 (Council Letter No. 18, page 368) has been carried and applicants for membership numbered 260 to 285, inclusive, are declared elected.

*122. Copyright of the N. F. VI.* A certificate of copyright registration, Entry: Class A, No. 93434, has been received from the Register of Copyrights, Library of Congress, Washington, D. C.

*123. Refunding Loan on Lot No. 7.* The following letter has been received from Dr. H. A. B. Dunning:

> "At the meeting of the A. PH. A. in Rapid City in 1929, I submitted a recommendation to the Council that authorization be given to purchase Lots 12, 13, 14, 15 and 7 in Square 62 of Washington, D. C., from the George Washington University, under the conditions set out in the communication which will be found on pages 959, 960 and 961 of the September 1929, A. PH. A. JOURNAL.
>
> "Lots 12, 13, 14 and 15 were necessary to complete our property, but the George Washington University was not willing to sell us these lots unless we would also purchase Lot No. 7. In view of the circumstances, the University agreed that if Lots 12, 13, 14 and 15 were paid for in cash, a mortgage note for $36,400.00 would be accepted for Lot No. 7 for five years, at 5½% interest, payable semi-annually, and this arrangement was approved by the Council.
>
> "The George Washington University has recently requested that this mortgage note be paid off because they need the proceeds in their building campaign. Arrangements have been made with the Maryland Trust Company, Baltimore, Maryland, for a loan of $36,400.00 for three years at 4%, payable quarterly, to pay the existing encumbrance.
>
> "I am requesting that the Council now authorize the proper officers to borrow the sum of $36,400.00 from the Maryland Trust Company for the purpose above stated and call attention to the fact that the proposed arrangement will mean a material reduction in the interest charge. The deed of trust requires a mortgage on all the property and the building. I can see no objection to this requirement, inasmuch as the mortage could be readily liquidated, if necessary, on account of the small sum involved."

Dr. Dunning has had the terms of the deed of trust examined by his legal advisor who approves the terms, and Chairman Hilton of the Council approves the refunding arrangement as outlined.

The District Title Insurance Company which company insured the title to the land owned by the ASSOCIATION will prepare and check the necessary papers.

(*Motion No. 57*) It is moved by Dunning that the Council of the A. PH. A. does hereby authorize C. W. Holton, treasurer, and E. F. Kelly, secretary, of the ASSOCIATION for the purpose of paying the existing encumbrance on the property, to borrow the sum of $36,400.00, said loan to be evidenced by a promissory note of this ASSOCIATION payable in three years with interest at 4%, payable quarterly, and to secure said note by executing a deed of trust in the usual form covering all of its land together with Building in Square 62 of the City of Washington, and does constitute and appoint S. L. Hilton its attorney in fact to acknowledge said deed of trust on behalf of this ASSOCIATION.

As the George Washington University requests the payment as promptly as possible a vote on this motion is called for. It will be considered as tentative if there is objection or if any members of the Council desire additional information or to submit comment.

*124. Applicants for Membership.* The following applications, properly endorsed and accompanied with the first year's dues, have been received:

No. 286, Kelsey H. Petro, 839 N. Kansas Ave., Topeka, Kans.; No. 287, Frank Milne, Pratt, Kans.; No. 288, Joseph D. McIntyre, Delaware Ave. & Vine St., Philadelphia, Penn.; No. 289, Edith M. Schofield, 26 S. Ohio Ave., Atlantic City, N. J.; No. 290, Paul J. Thomas, Vet. Admin. Frac., St. Cloud, Minn.; No. 291, Arthur P. Wyss, 800 E. Market St., Indianapolis, Ind.; No. 292, Wheaton Bernard Smith, 661 Knower St., Toledo, Ohio; No. 293, Walter H. Varnum, 801 Mass St., Lawrence, Kans.; No. 294, George N. Wilson, Mt. Pleasant, Tenn.; No. 295, Mary Imogene Shepherd, 20 E. Delaware Pl., Chicago, Ill.; No. 296, George F. Henriksen, 532 Fourth St., Camas, Wash.; No. 297, Peery Duderstadt, 4042 N. Francis St., Chicago, Ill.; No. 298, Albert Joseph Sica, 413 E. 202nd St., Bronx, N. Y. C.; No. 299, Herman Albert Timpf, 26 Hubbard Ave., Mt. Clemens, Mich.; No. 300, Gene B. Cook, 10 So. Wash., Iola, Kans.; No. 301, Catherine G. Glennon, 20 E. Delaware Pl., Chicago, Ill.; No. 302, Charles E. Green, Pittsfield, N. H.

(*Motion No. 58*) Vote on applications for membership in the AMERICAN PHARMACEUTICAL ASSOCIATION.

E. F. KELLY, *Secretary.*

LETTER NO. 20.

April 28, 1936.

*To the Members of the Council:*

*125. University of Southern California Student Branch.* The following application has been received together with the applications for membership and the dues for 1936:

"We, the undersigned, having conceived a favorable opinion of the aims and purposes of the AMERICAN PHARMACEUTICAL ASSOCIATION, and being of the opinion that we could successfully maintain a Student Branch of the Organization in the City of Los Angeles, in the State of California, hereby respectfully petition you to approve the formation of a Student Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION in said city and state, to be known as the University of Southern California Student Branch, and the By-Laws submitted herewith.

| | | |
|---|---|---|
| Harold Miller | Rose Ratner | Sam Presser |
| Albert H. Musick | Frances Fisch | Alberta Todd |
| Sidney Friedman | Ernest Yamaguchi | Charles Chase |
| Peter Bedrosian | Masaru Masuoka | Peggy Woods |
| Herman Weiner | Al Jannard | John Toshiyuki |
| Francis R. Daney | David Ostrom | Maurice Miller |
| Gordon D. Sherer | Philip W. Sanford | Andrew Kalick |
| Philip Lam | Henry Luis Roman | Hugh H. Bubar |
| Deran Tashjian | Charles Comstock | Gerald Hasimato |
| Leo Bittel | Aaron Land | Claus Amgren" |
| Mildred Sprinkle | George Sonoda | |

The following officers have been elected: *President,* Harold Miller; *Honorary President,* Albert Musick; *Vice-President,* David Ostrom; *Secretary,* Masaru Masuoka; *Treasurer,* Ernest Yamaguchi; *Faculty Advisors,* Harold R. Bowers and Alvah G. Hall.

The following is the Preamble and By-Laws:

In order to stimulate a greater professional and scientific interest in the students at the College of Pharmacy, University of Southern California, in the City of Los Angeles and vicinities, we, the undersigned, do hereby resolve to constitute ourselves into a Student Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION for the purpose of advancing the objects for which the body was founded. The branch hereby adopts for its guidance the Constitution and By-Laws of the AMERICAN PHARMACEUTICAL ASSOCIATION, and its members hereby subscribe to them.

ARTICLE I. *Members.* This branch shall consist of active and associate members.

ARTICLE II. *Active Members.* All members of the University of Southern California College of Pharmacy Student Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION shall be members regularly enrolled in Pharmacy in the University of Southern California College of Pharmacy, on signifying their intention of adhering to the provisions enumerated in the Preamble and in the Constitution of the AMERICAN PHARMACEUTICAL ASSOCIATION, shall be elected to active membership in this Branch.

ARTICLE III. *Associate Members.* Any person who is not an active member, but who manifests his interest either by contribution or active participation of work or research, scientific papers, or add to its financial resources, shall be termed an associate member but without the right to vote.

ARTICLE IV. *Officers.* The officers of the Branch shall be a president, vice-president, secretary and treasurer.

ARTICLE V. *Committees.* At the September meeting of each year or as soon thereafter as possible, the president shall appoint three standing committees as follows: A Committee on Program, to consist of three members; A Committee on Student Activities, to consist of three members; and a Committee on Membership, to consist of three members.

ARTICLE VI. *Executive Committee.* The officers of the branch and the chairmen of the

Standing Committees shall constitute the Executive Committee, to transact all the necessary business usually transacted by such a committee.

ARTICLE VII. *Meetings.* The meetings of the Branch shall be held at least once a month and as many more times as might seem advisable from the opening date of school each year to the close. Date of the meeting to be selected by the officers of the Branch.

ARTICLE VIII. *Quorum.* One-third the membership shall constitute a quorum.

ARTICLE IX. *Fiscal Year.* The fiscal year of the Branch shall be from the first of January until the first day of January of the following year.

ARTICLE X. *Elections.* The officers shall be elected by ballot by a majority, at the last meeting held in the college year, *i. e.*, from September to June, and shall be installed at the first meeting in September, and shall serve for one year, or until their successors have been elected. Nominations for officers shall be made at a meeting previous to the meeting at which the election is held. Written notice of both meetings shall be sent to all members.

ARTICLE XI. *Presiding Officers.* In the absence of the president, the next succeeding officer shall take the chair.

ARTICLE XII. *Secretary.* The secretary shall keep fair and correct minutes of the proceedings of the meetings and send reports of the same to the JOURNAL OF THE A. PH. A. as often as is required, and to such journals and newspapers as he may deem proper. He shall preserve on file, all reports and papers of every description presented to the branch, and shall be charged with the necessary business and scientific correspondence. He shall read all papers handed to him by the president for the purpose, shall call and record ayes and nays, whenever they are required to be called; shall notify the chairman of every standing and special committee of his appointment, giving him a list of his colleagues and stating the business upon which the committee is to act. He shall notify every member at least one week in advance of the time and place of the meeting.

ARTICLE XIII. *Treasurer.* The treasurer shall collect and take charge of the funds of the Branch and shall give receipts for the same. He shall pay no money except upon the order of the secretary countersigned by the president and accompanied by the proper vouchers. He shall present a statement of conditions at each December meeting of the Branch. He shall receive the amount of his expenses incident to the duties of his office.

ARTICLE XIV. *Order of Business.* (1) Reading of the minutes of the previous stated meetings; (2) Introduction of newly elected members; (3) Unfinished or deferred business; (4) New Business; (5) Program; (6) Nominations and elections; (7) Good and welfare; (8) Adjournment.

ARTICLE XV. *Miscellaneous.* Every proposition to alter and amend these By-Laws shall be submitted in writing at a stated meeting of the Branch, and may be balloted for at any subsequent stated meeting, when upon receiving the votes of three-fourths of the members present, it shall become a part of the By-Laws.

ARTICLE XVI. *Rules of Order.* On all points not specifically mentioned in the By-Laws governing this section, the By-Laws of the AMERICAN PHARMACEUTICAL ASSOCIATION shall take precedence over the other decisions on parliamentary rule.

(*Motion No. 59*) It is moved by Kelly that the application to establish a Student Branch in the College of Pharmacy, University of Southern California, and the proposed Preamble and By-Laws be approved.

*126. Will of George M. Beringer.* Recently the ASSOCIATION was advised by George M. Beringer, Jr., and the Camden Deposit & Trust Company, Executors and Trustees, of a proposed exchange of certain real estate, involving the payment of money to the estate, located in Merchantville, N. J., which will be submitted to the Court for ratification on May 4, 1936.

A copy of the Will was secured and the following bequest is quoted: "(*f*) AMERICAN PHARMACEUTICAL ASSOCIATION as a contribution to the invested maintenance fund for Pharmacy Headquarters Building, Twenty-five Hundred Dollars."

Mrs. Beringer has a life interest in the estate. A copy of the Will is being filed with other papers of the ASSOCIATION and a copy is being furnished to the Chairman of the Committee on Property and Funds.

*127. Reference Samples of Rennin.* Chairman Gathercoal writes that it becomes necessary to furnish Reference Samples of Rennin to those who will assay Rennin under the N. F. VI monograph for this product and that he has arranged for the supply of 60–10-Gm. vials of stand-

ardized Rennin, properly labeled at a cost which will be fully covered including containers and labels and transportation costs by a price of $1.00 per vial or $10.00 per dozen vials, transportation paid, to those who order the Reference Samples.

This is the only Reference Sample required in the N. F. VI and it is hoped that arrangements can be made to supply the Rennin samples with U. S. P. Reference Samples. The price recommended is the same as is charged for the U. S. P. Reference Samples.

(*Motion No. 60*) It is moved by Kelly that the 10-Gm. Reference Samples of Rennin, N. F. VI, be furnished at $1.00 per vial or at $10.00 per dozen vials, transportation paid, and that the cost for the samples, including transportation and other necessary expenses, be charged to the N. F. VI, and that the receipts from the sale of the samples be credited to N. F. VI.

*128. Use of Text of N. F. VI.* Chairman DuMez of the Committee on Publications has submitted the following recommendations on requests for permission to use the text of N. F. VI:

"It is recommended that permission to use portions of the text of the N. F. VI for comment in a book entitled 'Pharmacology, Materia Medica and Therapeutics' be granted to Charles Solomon on the same conditions under which permission was granted before and that the customary fee of $5.00 be charged."

"I have gone over the manuscript of Dr. McGehee's 'Textbook of Dental Pharmacology, Materia Dentica and Pharmaco-Therapeutics,' and find that the manner and extent of use of the text of the N. F. is satisfactory. I therefore recommend that permission to use said text be granted to the publishers, P. Blakiston's Son & Co., Inc., and that the usual fee of $5.00 be charged."

(*Motion No. 61*) It is moved by DuMez that Charles Solomon and P. Blakiston's Son & Co., be granted permission to use portions of the text of the N. F. VI in "Pharmacology, Materia Medica and Therapeutics" and in McGehee's "Textbook of Dental Pharmacology, Materia Dentica and Pharmaco-Therapeutics," respectively, with the customary acknowledgment and the usual fee of $5.00 in each case.

*129. Applicants for Membership.* The following applications, properly endorsed and accompanied with the first year's dues, have been received:

No. 303, George W. Fillauer, 930 E. Third St., Chattanooga, Tenn.; No. 304, Lucas Luis Velez, Carretera No. 9, Rio Piedras, P. R.; No. 305, George Miller, College Station Box 741, Pullman, Washington; No. 306, Juanichi Tomita, College Station Box 405, Pullman, Washington; No. 307, Harold Miller, 5632 Fernwood Ave., Los Angeles, Calif.; No. 308, Sidney J. Friedman, 1948 Judson St., Los Angeles, Calif.; No. 309, Peter Bedrosian, 942 W. 34th St., Los Angeles, Calif.; No. 310, Herman Weiner, 4216 S. Figueroa St., Los Angeles, Calif.; No. 311, Francis R. Daney, 349 W. 34th St., Los Angeles, Calif.; No. 312, Gordon D. Sherer, 1237 S. Bronson Ave., Los Angeles, Calif.; No. 313, Deran Tashjian, 4532 Abbey Pl., Los Angeles, Calif.; No. 314, Leo Bittel, 942 W. 34th St., Los Angeles, Calif.; No. 315, Mildred Sprinkle, 815 W. 37th St., Los Angeles, Calif.; No. 316, Rose Ratner, 10140 La Tuna Canyon Rd., Roscoe, Calif.; No. 317, Frances Fisch, 7013 Malabar St., Huntington Park, Calif.; No. 318, Ernest Yamaguchi, 923 W. 35th St., Los Angeles, Calif.; No. 319, Masaru Masuoka, 1016½ S. Catalina, Los Angeles, Calif.; No. 320, Al Jannard, 721 W. 30th St., Los Angeles, Calif.; No. 321, David Ostrom, 928 W. 37th St., Los Angeles, Calif.; No. 322, Philip W. Sanford, 837 W. 36th Pl., Los Angeles, Calif.; No. 323, Henry Luis Roman, 942 W. 34th St., Los Angeles, Calif.; No. 324, Charles Comstock, 5339 11th Ave., Los Angeles, Calif.; No. 325, Aaron Land, 1638 W. Adams St., Los Angeles, Calif.; No. 326, Sam Presser, 355 N. Breed St., Los Angeles, Calif.; No. 327, Alberta Todd, 604A E. Broadway, Los Angeles, Calif.; No. 328, Charles Chase, 721 W. 30th St., Los Angeles, Calif.; No. 329, Peggy Woods, 912 Roop St., Susanville, Calif.; No. 330, John Toshiyuki, 260 E. First St., Los Angeles, Calif.; No. 331, Maurice Miller, 5545 Fountain Ave., Los Angeles, Calif.; No. 332, Andrew Kalick, 1305 West Blvd., Los Angeles, Calif.; No. 333, Hugh H. Bubar, 3705 Diviggins St., Los Angeles, Calif.; No. 334, Gerald Hasimoto, 923 West 35th St., Los Angeles, Calif.; No. 335, Claus Amgren, 2212½ Berkeley St., Los Angeles, Calif.

(*Motion No. 62*) Vote on applications for membership in the AMERICAN PHARMACEUTICAL ASSOCIATION.

E. F. KELLY, *Secretary.*

LETTER NO. 21.

May 13, 1936.

*To the Members of the Council:*

*130. Use of Text of the N. F. VI.* Motions No. 55 and 56 (Council Letter No. 19, preceding) and Motion No. 61 (Council Letter No. 20, preceding) have been carried and the parties to whom permission was granted have been so advised.

Chairman DuMez of the Committee on Publications writes:

> "I have carefully reviewed the material from the N. F. VI which Dr. Irwin Sugar requests permission to use in preparation of a reference book for Chiropodists, and find it to be entirely satisfactory. Only about 36 formulas are given and directions for making the preparations are omitted in all cases.
>
> "I, therefore, recommend to the Council that permission be granted to Dr. Irwin Sugar to use portions of the text of the N. F. VI for comment in a reference book for Chiropodists."

(*Motion No. 63*) It is moved by DuMez that Irwin Sugar, Chicago, Ill., be granted permission to use portions of the text of the N. F. VI in a reference book for Chiropodists with the customary acknowledgment and at the usual fee of $5.00.

*131. Refunding Loan on Lot No. 7.* Motion No. 57 (Council Letter No. 19, preceding) was carried and Treasurer Holton and Secretary Kelly completed the loan from the Maryland Trust Company on May 1, 1936. S. L. Hilton acknowledged the note and deed of trust as attorney in fact for the ASSOCIATION. The loan formerly held by the George Washington University was paid off. The District Title Insurance Company prepared and checked all of the papers and attended to releasing the former deed of trust and recorded the new one, and the charges amounted to $107.95, including legal fees.

*132. Election of Members.* Motion Nos. 58 (Council Letter No. 19, preceding) and 62 (Council Letter No. 20, preceding) have been carried and applicants for membership numbered 286 to 335, inclusive, are declared elected.

*133. University of Southern California, Student Branch.* Motion No. 59 (Council Letter No. 20, preceding) has been carried and the application and the Preamble and By-Laws are approved.

*134. Reference Samples of Rennin.* Motion No. 60 (Council Letter No. 20, preceding, has been carried and the samples will be handled as directed.

*135. Corrections in N. F. VI.* Attached is a list of 54 corrections approved by the Committee on National Formulary for issuance at this time.

Twenty-two of the proposed corrections were submitted in Council Letter No. 17, page 365, and approved. They are as follows: Pages 5—line 4, 5—line 26, 7—line 36, 41—line 6, 45—line 27, 159—line 8, 164—line 13, 250—line 25, 353—line 14-A, 372—line 39, 494—line 11, 515—line 33, 515—line 44, 535—line 27, 536—line 25, 537—line 2, 540—line 24, 541—line 12, 542—line 2, 543—line 53, 545—line 38 and 545—line 39.

It is planned to issue this list of corrections in printed sheets, 6 x 9 inches, in the form herewith submitted, and printed on one side, and so arranged that they can be inserted in the front of the book or that each correction can be cut out and pasted over the material it is to replace.

> It is also planned to send the following bulletin to the pharmaceutical, medical, dental, veterinary, hospital and chemical publications, to secretaries of pharmaceutical associations and state boards, to schools and colleges of pharmacy, to member firms of the A. D. M. A., A. P. M. A., N. W. D. A., F. W. D. A. and the Proprietary Association:
>
> "Since the National Formulary, Sixth Edition, was issued on December 16, 1935, many interested persons have read the book very critically, and quite a number of corrections in the text have been suggested.
>
> "These proposed corrections included simple typographical errors, a few errors in the tolerance figures for the alcoholic content of certain galenical preparations, and a few changes in dose statements.

"The Committee on National Formulary has given each of the suggestions very careful consideration and has compiled a list of 54 corrections to be made in the first printing of the N. F. VI, bearing official coupons with serial numbers from 100,001 to 125,000. The corrections have been approved by the Council of the AMERICAN PHARMACEUTICAL ASSOCIATION and will be made in subsequent printings of N. F. VI.

"A list of these corrections, printed on one side of the sheet, is available, without cost, and is so arranged that the sheets can be inserted in the front of the N. F. VI or that each correction can be cut out and pasted over the wording it is to replace.

"Requests for the list of Corrections in N. F. VI may be sent to Mack Printing Company, Easton, Penna., or to the AMERICAN PHARMACEUTICAL ASSOCIATION, 2215 Constitution Avenue, Washington, D. C., and *must be accompanied by a self-addressed stamped envelope* to insure delivery."

(*Motion No. 64*) It is moved by Kelly that the proposed corrections, Items 23 to 54, inclusive, in the text of N. F. VI be approved, that the corresponding corrections be made in the plates before the second printing of the N. F. VI and that a list of the approved corrections in the form above indicated and without charge be issued covering the first printing.

*136. Applicants for Membership.* The following applications, properly endorsed and accompanied with the first year's dues, have been received:

No. 336, Mancil Havren White, 3001 Live Oak St., Dallas, Texas; No. 337, Weyland D. Sears, 816 Seward St., Evanston, Ill.; No. 338, Bernice Berry Brown, 4301 Oak Lawn Ave., Dallas, Texas; No. 339, Marvin Bryant Neal, Crossett, Ark.; No. 340, Isabelle Seismann, 10111 118th St., Richmond Hill, N. Y.; No. 341, Saul Asnis, 2784 W. 36th St., Brooklyn, N. Y.; No. 342, Ettore John Graziano, 9465 Ridge Blvd., Brooklyn, N. Y.; No. 343, John O'N. Casey, 2100 Darby Road, So. Ardmore, Upper Darby, Penna.; No. 344, D. P. Lillich, Dundalk Bldg., Dundalk, Md.; No. 345, Charles Everett Erickson, Loomis, Nebr.; No. 346, Leonard Eugene McHugh, 91 N. Edgewood Ave., La Grange, Ill.; No. 347, Herbert N. van Nostrand, 191–202—119th Ave., St. Albans, N. Y.; No. 348, Isadore Wexler, 2 Forsythe Place, Newburgh, N. Y.; No. 349, William Julius Smith, 114 N. Columbia St., Chapel Hill, N. C.

(*Motion No. 65*) Vote on applications for membership in the AMERICAN PHARMACEUTICAL ASSOCIATION.

*137. Request for Additional Compensation on Account of Printing and Binding the N. F. VI.* The Mack Printing Company have submitted, after a personal visit to the ASSOCIATION'S office, a request for the following compensation in addition to the bill submitted in accordance with the terms of the contract:

| | |
|---|---|
| To cover additional cost for overtime and double time, for night and Sunday work, required to meet a shortened delivery date | $322.71 |
| To cover an 8% increase in production cost affecting composition and presswork only, arising from compulsory wage increase by Federal Legislation | 321.43 |
| To cover interest on the paper investment made 2½ years prior to the issue of the N. F. VI | 299.10 |
| | $943.24 |

The Company has submitted a detailed review of the reasons for these additional expenses which are summarized as follows:

The contract revision in 1934 included a 20% estimated increase in wages whereas the actual increase proved to be 36% due to the scale of wages, the decrease in hours of the working week and the expenses of Code compliance.

The original contract was based on a production period of sixty days whereas it became necessary to produce the book in forty-five days so that it would be issued in 1935 which required overtime at a higher rate of pay.

The necessary paper stock was purchased in 1933 when the original contract was signed. The paper cost $1994.07 and would have cost, when used, not less than $2653.11. It was not

expected that the work would be delayed so long and a 6% interest carriage charge is requested since the paper was paid for when purchased.

For the information of the Council, a similar request was submitted on account of the U. S. P., was investigated by a special committee and approved by the Board.

The request on account of the N. F. VI with detailed explanation was submitted to Chairman DuMez of the Committee on Publications who wrote as follows:

> "As I understand it, the main point at issue is whether or not we wish to stand strictly by the contract or whether we desire to be somewhat lenient with the Mack Printing Company. The latter will have to be disposing of a good many National Formularies for us in the next ten years and it is my opinion that we cannot afford to antagonize them. I would therefore recommend honoring their request in full if necessary."

and to Acting Chairman Hilton of the Committee on Finance who approved the request.

(*Motion No. 66*) It is moved by Kelly that the request of the Mack Printing Company for additional compensation on account of the printing and binding of the N. F. VI, as submitted above, be approved and that they be paid the amount requested, $943.24. A vote on the motion will be called for in about ten days.

*138. American Association for the Advancement of Science.* The following letter has been received from Dr. Henry B. Ward, Permanent Secretary:

> "At a meeting of the executive committee held in Lancaster, Pa., April 18th and 19th, the committee approved the transfer of the AMERICAN PHARMACEUTICAL ASSOCIATION in the list of affiliated societies from the Section on Chemistry to the Section on Medical Sciences."

The AMERICAN PHARMACEUTICAL ASSOCIATION was originally affiliated with Section C (Chemistry) and with Section N (Medical Sciences) and was listed as affiliated with the former.

It will be recalled that the A. A. A. S. recently created sub-sections of Section N for Dentistry and for Pharmacy, and the A. PH. A. is therefore listed as affiliated with that section.

The Executive Committee of the A. A. A. S. has approved the appointment of the following members to act as an executive committee for the sub-section on pharmacy: Dr. John C. Krantz, Jr., *Chairman*, Dean R. A. Lyman and Dean Wortley L. Rudd.

*139. American Physical Society.* This Society holds its annual meetings at the Bureau of Standards and at the National Academy of Sciences. Some time ago officials of the Society inquired if one of its sections could meet in our Building on Saturday, May 2nd, and were assured that this would be entirely agreeable.

The following letter has been received from Dr. W. L. Severinghaus, Secretary of the Society:

> "As you know the American Physical Society was confronted with the largest program in its history at its Washington meeting on April 30, May 1 and 2, 1936. We were at a loss to know where to hold our meetings and you very kindly came to our rescue and offered us your meeting room in the Pharmaceutical Building. The Society passed the following resolution which I transmit to you with pleasure:
>
> "*Resolved*, that the American Physical Society express to the AMERICAN PHARMACEUTICAL ASSOCIATION deep appreciation of its courtesy in offering to the Society the use of its auditorium for the meetings on Saturday morning and afternoon."

E. F. KELLY, *Secretary.*

CORRECTIONS IN N. F. VI.*[1]

To Be Made in Books No. 100,001 to No. 125,000.

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* April 27, 1936, *National Formulary Bulletin*, pages 2291–2293.

[1] *Corrections in N. F. VI.*—Through oversight, the list of 54 corrections was not attached to Council Letter No. 21, see item No. 135, page 471. The list is attached hereto.

E. F. KELLY, *Secretary.*

| Page. | Line. | |
|---|---|---|
| v | 4 | *Change* Phar. M. *to* Ph. M. |
| v | 26 | *Change* Phar.M. *to* Ph.M. |
| 7 | 36 | *Change* One liter equals 1000.27 cc. *to* One liter equals 1000.027 cc. |
| 33 | 22–26 | *Change to:* Ampuls of Dextrose contain a sterile solution of 50 Gm. of dextrose in a sufficient quantity of ampul water to make 100 cc., unless another concentration of the solution is stated on the label, and yield an amount of anhydrous dextrose, $C_6H_{12}O_6$, corresponding to not less than 86 per cent and not more than 96 per cent of the labeled amount of dextrose. |
| 35 | 16–18 | *Change to:* solution is stated on the label, and yield an amount of anhydrous emetine hydrochloride, $C_{29}H_{40}O_4N_2.2HCl$, corresponding to not less than 84 per cent and not more than 92 per cent of the labeled amount of emetine hydrochloride. |
| 35 | 39 | *Change* 0.006794 Gm. *to* 0.005533 Gm. |
| 35 | 40 | *Change* $C_{29}H_{40}O_4N_2.2HCl.7H_2O$ *to* $C_{29}H_4O_{10}N_2.2HCl$. |
| 41 | 6 | *Change* contained *to* contain. |
| 45 | 27 | *Change* 0.005846 Gm. *to* 0.005845 Gm. |
| 50 | 39–41 | *Change to:* Place 10 cc. of Water in a clean test-tube and add 2 drops of methyl red $p_H$ indicator: no orange color develops, indicating a hydrogen-ion concentration of not less than $p_H$ 5.8. Another 10-cc. portion of Water does not show a pink color. |
| 52 | 10–14 | *Change to:* Macerate a weighed amount of the recently cut and partially dried dormant twigs of *Hamamelis virginiana* for about 24 hours in about twice their weight of water; then distil until not more than 850 cc. of distillate is obtained for each 1000 Gm. of the twigs taken; add 150 cc. of alcohol to each 850 cc. of distillate; mix thoroughly. |
| 52 | 31 | *Change* 13 to 15 *to* 14 to 15. |
| 53 | 33–37 | *Change to:* Place 10 cc. of Redistilled Water in a clean test-tube and add 2 drops of methyl red $p_H$ indicator: no orange color develops, indicating a hydrogen-ion concentration of not less than $p_H$ 5.8. Another 10-cc. portion of Redistilled Water does not show a blue color on the addition of 5 drops of bromthymol blue $p_H$ indicator, indicating a hydrogen-ion concentration of not more than $p_H$ 7.0. |
| 66 | 47 | *Change* 3.6724 Gm. *to* 3.7473 Gm. |
| 68 | 26 | *Change* 1 cc. *to* 4 cc. |
| 77 | 21 | *Change* didymium *to* neodymium, praseodymium. |
| 89 | 45 | *Omit* "Lutein;" transfer *or* to between "Extract" and "Colora Lutea." |
| 117 | 3 | *Change* 21 to 24 *to* 24 to 28. |
| 112 | 21 | *Change* 22 to 24 *to* 23 to 26. |
| 122 | 13 | *Change* 1 cc. *to* 0.1 cc. |
| 138 | 4 | *Omit* 1 Gm. of the Extract represents 2 Gm. of aloe. |
| 159 | 8 | *Change* 9.27 Gm. *to* 0.27 Gm. |
| 162 | 3 | *Change* 57 to 63 *to* 52 to 57. |
| 164 | 5 | *Change* 0.1 Gm. *to* 0.1 cc. |
| 164 | 13 | *Change* in each 100 cc., 3.75 U. S. P. *to* in each 0.1 cc., 3.0 U. S. P. |
| 180 | 31 | *Change* 12 to 18 *to* 17 to 21. |
| 187 | 3 | *Change* **Gel. Ephed. to Gel. Ephed. Sulf.** |
| 205 | 34 | *Change to:* Average dose: Metric, 1 Gm.—Apothecaries, 15 grains. |
| 210 | 35 | *Change* 12 mm. *to* 10 mm. |
| 244 | 25 | *Change* 8 Gm. *to* 6 Gm. |
| 250 | 25 | *Change* Compositæ *to* Composita. |
| 317 | 38 | *Change* the walls *to* the cell walls. |
| 353 | 14-*a* | *Add* **Distilled Water,** a sufficient quantity. |
| 372 | 39 | *Change* 10 cc. *to* 100 cc. |
| 393 | 36-*a* | *Add:* Dogs, 0.2 cc. per Kg. of body weight. |
| 397 | 26 | *Change* 57 to 63 *to* 63 to 69. |

| | | |
|---|---|---|
| 397 | 27 | *Change to:* Average dose: Metric, 0.5 cc.—Apothecaries, 8 minims. |
| 424 | 3 | *Omit* Analgesic Balm. |
| 434 | 3 | *Change* contain *to* each contains. |
| 439 | 38 | *Change* Potassium Hydroxide *to* Sodium Hydroxide. |
| 475 | 20 | *Omit* (*Paris Green*). |
| 494 | 11 | *Change* March 1 *to* June 1. |

INDEX.

| Page. | Column. | Line. | |
|---|---|---|---|
| 515 | 2nd | 33 | *Change* 473 *to* 474. |
| 515 | 2nd | 44 | *Change* 476 *to* 475. |
| 535 | 2nd | 27 | *Change* 313 *to* 131. |
| 536 | 2nd | 25 | *Change* Compositæ *to* Composita. |
| 537 | 2nd | 2 | *Change* Mercurous Chloride, Iodide *to* Mercurous Iodide. |
| 540 | 1st | 24 | *Change* 475 *to* 479. |
| 541 | 1st | 12 | *Change* 434 *to* 435. |
| 542 | 2nd | 2 | *Change* Potassium Acetate, Hydroxide, *to* Potassium Hydroxide. |
| 543 | 2nd | 53 | *Omit* Red, Phenol, Test Solution . . . . . 482. |
| 544 | 1st | 40 | *Change* Rocella *to* Roccella. |
| 545 | 2nd | 38 | *Change* 208 *to* 308. |
| 545 | 2nd | 39 | *Change* 340 *to* 240. |

## AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE, MEETING WILL BE HELD IN ROOM K 307, SCHOOL OF MEDICINE AND DENTISTRY, UNIVERSITY OF ROCHESTER.

(N) MEDICAL SCIENCES, ($N_2$) PHARMACY, THURSDAY, JUNE 18, 1936—9.00 A.M.

John C. Krantz, Jr., *Chairman.* A. B. Lemon, *Secretary.*

Program.

1. "A Comparison of the Pharmacological Syndromes of Ergostetrine (Ergometrine, Ergotocin, Ergonovine, Ergobasine) and the Ergotoxine-Ergotamine Group of Ergot Alkaloids." By Marvin R. Thompson, School of Pharmacy, University of Maryland. 10 min.

2. "Further Observations on the Use of Pigeons in the Standardization of Digitalis Bodies." By H. B. Haag, Medical College of Virginia. 10 min.

3. "Differential Pharmacognosy of the Two Lobes of the Pituitary Gland." By Heber Youngken, Massachusetts College of Pharmacy. 10 min.

4. "Hydrolysis of Sucrose Solutions and Its Significance in the Preservation of Pharmaceutical Syrups." By H. V. Arny and W. C. Mende, Columbia U., College of Pharmacy. 10 min.

5. "Observations on the Assay of Vitamins B and $B_2$." By F. K. Riggs and A. Beaty, Rutgers University. 10 min.

6. "Variations in the Electrophoretic Behavior of Gelatin Protected Silver Halide Solutions." By L. S. Tice and W. G. Batt, Philadelphia College of Pharmacy and Science. 10 min.

7. "Titration of Iodides and Iodine in Common Solution." By Wm. Reindollar, Bureau of Chemistry, Maryland State Department of Health. 10 min.

8. "Further Studies on the Effect of Cyanides in Rat Sarcoma." By John C. Krantz, Jr., Ruth Musser, C. Jelleff Carr and Wm. G. Harne, School of Medicine, U. of Maryland. 10 min.

9. "Studies on the Metabolism of Dextrose Fragments." By John C. Krantz, Jr., Ruth Musser, C. Jelleff Carr, T. Nelson Carey and Frances Beck, School of Medicine, University of Maryland. 10 min.

10. "Variations in the Toxicity of Strychnine." By James C. Munch, Temple University. 10 min.

11. "The Minimal Lethal Dose for Fluidextract of Ergot, Ergotoxine and Ergonovine." By E. I. Evans, University of Chicago. 10 min.

12. "The Involution of the Mouse Uterus." By Richard A. Deno, Medical College of Virginia. 10 min.

## GOLDEN ANNIVERSARY ADDRESS.*

BY ROBERT P. FISCHELIS.

This occasion is at once the Anniversary of fifty years of continuous activity by Dean Gregory in a profession serving the public health and the Golden Anniversary of the college which can rightfully be termed his "lengthened shadow." In point of service, Dr. Gregory is the Dean of Deans of the seventy odd American Colleges of Pharmacy. The esteem in which he is held in the realm of pharmacy is due to his charming personality, his patience, tolerance, keen wit and gracious manner, as well as to his great ability as an educator and administrator.

Within the span of years covering Dr. Gregory's association with pharmacy, profound changes have occurred in the methods of medical practice, which have been reflected in the practice of pharmacy. About the time the Buffalo College of Pharmacy was organized, Pasteur was completing the researches which led to the development of successful vaccination against anthrax and rabies. Synthetic Chemistry was just beginning to produce the coal tar drugs which have assumed such great importance in the field of medication. Antipyrine, one of the earliest of these, was first prepared in 1884. Diphtheria Antitoxin was discovered in 1889, the X-Ray in 1895 and Radium in 1898.

The first Federal Food and Drug Act was passed in 1906, the Harrison Anti-Narcotic Law in 1914, and the National Prohibition Law of 1919 made its exit some fourteen years later. The first State law requiring pharmacists to be college graduates was passed by the State of New York in 1904. These are but a few of the outstanding events which have passed in parade before the eyes of the guest of honor. His influence upon nearly 2000 pharmacy graduates, his activity within the profession and his work in behalf of the University of Buffalo, have made him a figure of national importance in American Pharmacy.

Anniversaries are occasions for evaluating the past and contemplating the future. As the College of Pharmacy of the University of Buffalo enters its second half-century of service, conditions in the practice of pharmacy challenge the best thought and ability of its leaders. We see the actual compounding of medicines taken over by larger manufacturing units and the reduction of the average retail pharmacist to the position of a dispenser of ready-made medicines.

Without adequate control over advertising and production of their remedies, the public is being educated by manufacturers to medicate itself, and the use of possibly harmful drugs, without medical or pharmacal advice, is being encouraged to the point where the public health demands some type of supervision. Passage of a revised Federal Food and Drug Law giving the U. S. Food and Drug Administration control over advertising, requiring the disclosure of the formulæ of proprietary remedies and strengthening the public control over the drug industry, is essential to the public welfare and should be forthcoming at this session of Congress.

The possibility of absorption of the functions of private medical and pharmaceutical practice by the State, through some form of Health Insurance, is no longer academic. It is seen by some as the only way out of the difficulty of providing adequate service to all the people at a price they can afford. Enrollment of freshmen in 68 colleges of pharmacy throughout the United States dropped 53% between 1924 and 1933. The number of graduates in pharmacy has decreased from one for every 17 drug stores in 1924 to one for every 25 drug stores in 1933. The so-called one-man drug store operated by a single registered pharmacist working 96 hours per week or more is unable to cope with the type of competition offered by chain organizations. However, several pharmacists associating themselves for the purpose of conducting a professional establishment may be able to cope with the problems of high rentals, quick merchandising and store management, while providing the indispensable professional service which the public still prefers to receive from private practitioners.

Better organization of professional pharmacists with county and local units becoming integral parts of the National Association of Retail Druggists and the AMERICAN PHARMACEUTICAL ASSOCIATION, and observance of a stringent code of ethics which will refuse to subordinate professional service to commercial exploitation, will assure survival of the private practice of pharmacy.

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* Brief summary of an address at the Golden Anniversary Banquet of the College of Pharmacy, University of Buffalo, April 22, 1936.

# EDITORIAL NOTES

## RECOGNITION OF PHARMACISTS BY SENATE BILL 4390.

In the April number of the JOURNAL reference was made to the progress of S. 4390, introduced by Senator Sheppard and the support given by the Surgeon General. The active interest of the Senator and of the War Department is appreciated. The Bill has now proceeded so that it is on the Union Calendar and there is reasonable assurance for enactment.

Congressman Charles I. Faddis, of Pennsylvania, who has charge of the measure for the House Committee on Military Affairs, concluded his statement for the Committee by saying: "The Committee feels that, under present conditions, proper recognition commensurate with education and qualification of the pharmacists connected with the Medical Corps of the United States Army is lacking. This makes it impossible to secure pharmacists of the proper professional qualifications to fill this most important function connected with the Medical Corps. This legislation will remedy the present condition and will, without additional cost, add to the efficiency of the Medical Corps and give these specialists the recognition in rank to which they are entitled."

This is bringing near conclusion efforts of many years by the AMERICAN PHARMACEUTICAL ASSOCIATION and the result of coöperation by the Senate and House, the Army and the Surgeon General. It is a forward step for pharmacists.

## A QUESTION RELATIVE TO COCAINE ANESTHESIA.

An interesting letter appears in the *New York Times* of May 24th, by Dr. Carl Koller. Aside from answering the question of fact the latter gives historical data. While there is evidence on the subject, it is a source of satisfaction that Dr. Koller, who is well along in years, can answer the question in a personal communication.

In this connection, reference may be made to the PROCEEDINGS, A. PH. A., of 1885 and *Squibb's Ephemeris*.

## CALL OF THE SCIENTIFIC SECTION, A. PH. A.

The 84th annual meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION will be held in Dallas, Texas, during the week of August 24th.

The officers of the Scientific Section appreciate the interest shown in past years, and are now making an appeal for support to make the Dallas meeting a success.

The Scientific Section will hold several sessions, and for the officers to plan the program we should have, as early as possible, the titles of the papers which contributors plan to present, and also short abstracts of same. When submitting the title please advise the secretary whether you will present the paper in person or by title, also whether a lantern will be required for presentation. Copies of the abstracts must be in the hands of the secretary at least three weeks before the meeting. Copies of all papers should be in the hands of the secretary before the meeting.

The By-Laws provide that papers shall be presented in duplicate so that one copy will be available for publication and the other copy referred to the Committee on Ebert Prize. In writing the paper the author should follow the procedure outlined in THIS JOURNAL, page 484. The By-Laws also require that before publication all papers presented to the Scientific Section must be passed by the Board of Review of Papers. Authors can assist the Board of Review if, when writing the original paper, they will eliminate any non-essential material, presenting the subject in a short, concise form and being particularly careful to avoid duplication of experimental work, statements, etc.

H. M. BURLAGE, *Chairman*, Scientific Section.

FRANCIS E. BIBBINS, *Secretary*, Scientific Section, 5840 Washington Blvd., Indianapolis, Indiana.

## NARCOTIC CONFERENCE.

The United States will be represented by delegates in Geneva for the study of illicit narcotic drugs. The convention meets June 8th and Stuart J. Fuller, Assistant Chief of the Divison of Far Eastern Affairs, H. J. Anslinger, Commissioner of Narcotics and Frank X. Ward, Assistant to the Legal Adviser, are delegates.

## UNIVERSITY OF TEXAS COLLEGE OF PHARMACY.

The Pharmacy College will have a display at the University Centennial Exposition in Austin, featuring drugs of the scriptures, early pharmaceutical apparatus and indigenous remedies.

## PERSONAL AND NEWS ITEMS.

**Dr. Ibrahim Ragab Fahmy,** of the Faculty of Medicine, Cairo, has favored us with a report of the Pharmacognosy Department of the Egyptian University. The report shows plants and scenery of the section in connection with interesting descriptions.

We are indebted to **I. R. Fahmy**[1] for a reprint of "Some Observations on the Action and Methods of Standardization of Hashish."

**Dr. A. B. Lemon** is the new dean of Buffalo University School of Pharmacy. He joined the faculty in 1916 and has been its secretary for the past 17 years. From 1924–1926, he collaborated with Dr. W. W. Charters in the study and compilation of "Basic Material for a Pharmaceutical Curriculum." He is active in pharmaceutical organizations, in examination studies and research promotions.

**Dr. Marvin R. Thompson** has been elected to honorary membership in Rho Chi and was presented with a key and certificate at the Baltimore meeting on May 18th.

**Joseph Price,** "Holiday House," Wellfleet, Mass., has donated, through C. Herbert Packard, an interesting illustrated volume on Henry Troth, one of the pioneers among American pharmacists. It is interesting to note such names in the genealogy as Joseph Price, Sarah Remington, etc. The Price family of Salem included many eminent pharmacists who were preceptors of other generations of pharmacists, such as Henry Estabrook, S. A. D. Sheppard, etc.

**Mrs. F. W. Meissner** has favored us with an autobiography of her late husband, a biography of Leo Eliel, by Mr. Meissner and Miss Backus, and a brief history of all the drug stores in La Porte. The Meissner Pharmacy will be continued by the family; they are: Roger, of New York City; Clement, of Denver, Colorado; Miss Virginia, of La Porte; Frederick, known to radio listeners as "Fritz Clark."

**Bernard E. Read,** of the Department of Pharmacology, Peiping Union Medical College, has favored us with "Chinese Materia Medica," Animal Drugs, and Avian Drugs. Also "Chinese Medicinal Plants." Dr. Read is the author of these publications, published by the *Peking Natural History Bulletin.*

The following were named members of the executive committee for the subsection on pharmacy of the American Association for the Advancement of Science: **Dr. John C. Krantz, Jr.,** *Chairman,* University of Maryland School of Medicine, Baltimore, Md.; **Dean R. A. Lyman,** University of Nebraska, Lincoln, Nebr.; **Dean Wortley F. Rudd,** School of Pharmacy, Medical College of Virginia, Richmond, Va.

[1] Pharmacognosy Department, Faculty of Medicine, Cairo.

**Professor Charles F. Poe,** of *Pharmaceutical Chemistry,* is mentioned in the lead article of the March issue of the *Atlantic Monthly,* as a result of his association in Paris with James Abbe, international press photographer and news correspondent. The story is entitled "I, Patience," written "By Herself." Patience is the eleven-year old daughter of Mr. Abbe.

**Dr. James M. Dille** has recently been appointed associate professor in the College of Pharmacy at the University of Washington, under Dean C. W. Johnson. Doctor Dille will be in charge of the reorganization and development of the Department of Pharmacology. A course in biological assay with experimental work on the assay of the pharmacopœial and of other preparations is to be begun and upon the completion of the new Pharmacy-Chemistry building, a laboratory course in experimental pharmacology will be organized.

Doctor Dille has been in the Department of Pharmacology of Georgetown University School of Medicine for the past three years and previously was instructor of Physiology in the College of Pharmacy at the University of Nebraska. He will begin his new duties in September of this year.

**Dean R. A. Lyman,** of the College of Pharmacy of the University of Nebraska, represented the American Association of Colleges of Pharmacy at the 19th annual meeting of the American Council on Education, held in Washington, on May 1st and 2nd. The meeting was attended by nearly four hundred representatives.

Two members of the first graduating class of the Brooklyn College of Pharmacy, Long Island University, were among the more than 500 persons at the 50th anniversary celebration held on April 21st at the Towers Hotel in Brooklyn, N. Y. The two old-timers were **Dean William C. Anderson** and **Louis Berger.**

**Senator Morris Sheppard,** speaking for the amendment to S.4390 said in part: "At

present those performing the duties of pharmacists in the Medical Administrative Corps are taken from among the enlisted men in the Medical Corps, and they have at first no special knowledge or technical qualifications to fit them for the work. The bill requires that before men shall hereafter be appointed to this position of pharmacist they must be graduates of recognized schools or colleges of pharmacy having four-year courses. The bill adds nothing to the cost of administration but merely provides that as vacancies occur in the position of pharmacists in the Medical Corps they shall be filled by men specially qualified. This will give the Army a group of pharmacists with thorough technical training and attainment."

**Dean A. R. Bliss, Jr.,** of the School of Pharmacy, Howard University, Auburn, Ala., in coöperation with **Prof. Lewis W. Lohr,** has established a service which is designed to help raise the professional standard of pharmacy and give pharmacists in Alabama information on problems met with in their professional practice.

A statue of Hippocrates was unveiled in the court of the new laboratories of the University of Athens, Greece, during the session of the International Congress of Biology.

**Dr. Wm. M. Cogan,** dean of Georgetown University School of Dentistry, was given a surprise party by his students on the occasion of his 80th birthday.

**Hugh Craig,** associate editor of the *Druggists Circular*, delivered the address to the graduates of Columbia University College of Pharmacy.

**William B. Day,** after a service of thirty years as secretary of the Illinois Pharmaceutical Association and secretary of its Executive Committee, has retired. He was presented by Governor Horner, for the Association, with a handsome gold wrist watch. The Association also elected him *Honorary President* of the Association for life, the office being created for him by vote; tributes by members were paid the faithful officer.

## OBITUARY.

### ELIE HENRY LA PIERRE.

Elie Henry La Pierre, *Honorary President* of the AMERICAN PHARMACEUTICAL ASSOCIATION, 1930–1931, died at his home in Cambridge, Mass., May 2nd. He was born February 20, 1859, in Wolcottville (Torrington), Conn., the son of Elie F. and Sarah La Pierre. The family moved to Burlington, Vt., where the youth began his education. After his father's death, the family removed to Cambridge, where the young man's education was continued and here he resided until his demise.

After serving an apprenticeship in pharmacy with J. Ward Hill, he entered Massachusetts College of Pharmacy and graduated with the class of 1880. The Hill pharmacy was purchased by Bayley and Richardson and the graduate pharmacist continued in the employ of the firm until he purchased the pharmacy. He served the community as employee and owner for about sixty-five years—in 1921, he celebrated the 50th anniversary of the beginning of his service with Mr. Hill. (See sketch in JOURNAL, A. PH. A., for December 1930.)

Professor La Pierre became a member of the AMERICAN PHARMACEUTICAL ASSOCIATION in 1892 and served on a number of important committees. He was elected vice-president of the American Conference of Pharmaceutical Faculties in 1909 and due to the death of President Searby, became acting president, presiding at the Richmond meeting.

In 1885, he joined the Massachusetts Pharmaceutical Association and served as its president in 1904–1905. Soon after graduation, Professor La Pierre became active in the affairs of Massachusetts College of Pharmacy and, in 1892, member of the faculty, holding positions, successively, as instructor in Materia Medica and Botany, professor of Applied Pharmacy, instructor in Theoretical Pharmacy, professor of Theoretical and Applied Pharmacy and professor of Pharmacy.

The La Pierre Drug Company, of which the deceased was president, owned several stores in Cambridge and one in Boston; he took an active part in civic affairs, served for many years on the Board of Health, as a trustee of the Cambridge Hospital and in other promotions. "With all his varied activities, Professor La Pierre remained a professional pharmacist."

The deceased is survived by his widow, two daughters and several grandchildren.

### LEWIS WILLIAM McCONNELL.

L. W. McConnell, member of the AMERICAN PHARMACEUTICAL ASSOCIATION since 1904, died of a heart attack April 24th. Mr. McConnell had been in poor health for several years. He was a pioneer pharmacist of McCook, Nebraska, was highly regarded in the state, active in the affairs of the state association and held life membership in the N. A. R. D.

## SOCIETIES AND COLLEGES.

### SOCIETY OF PHARMACOLOGY AND THERAPEUTICS.

The following officers of the American Society for Pharmacology and Experimental Therapeutics were elected at the recent annual meeting held at Washington: *President*, V. E. Henderson; *Vice-President*, O. H. Plant; *Secretary*, E. M. K. Geiling; *Treasurer*, C. M. Gruber; *Councilors*, Professor C. W. Edmunds and G. Wallace; *Representative on the National Research Council*, W. deB. MacNider.

### MINNESOTA PHARMACEUTICAL ASSOCIATION.

Chairman Lillis announced the results of the Minnesota election by mail to be as follows, the men named to assume office at the completion of 1937 convention of the state association in St. Paul. The new officers: *President*, Jesse B. Slocumb, St. Paul; *Vice-Presidents:* George Kermott, Duluth; Len E. Merwin, Minneapolis; Fred G. Kustermann, St. Paul; *Secretary*, A. Roy F. Johnson, Minneapolis; *Treasurer*, Charles T. Heller, Jr., St. Paul; *Executive Committeeman:* Roy G. Paulson, Fairmont. Mr. Paulson will succeed Charles A. Anderson, who is this year chairman of the Executive Committee. Theodore A. Arneson and Joseph Vadheim complete the membership of this committee.

### IDAHO PHARMACEUTICAL ASSOCIATION.

The dates for the Idaho convention at Idaho Falls have been changed to June 22nd–23rd instead of June 15th–16th, as originally announced.

### AMERICAN MEDICAL ASSOCIATION.

Dr. James S. McLester, Birmingham, Ala., delivered the presidential address at the annual meeting of the American Medical Association in Kansas City (May 11th–15th). President-Elect J. Tate Mason was prevented from attending the meeting. Dr. John H. J. Upham, dean of the medical school of Ohio State University, is now *President-Elect* of the Association.

### UNIFORM NARCOTIC LAW.

The bill to bring the District of Columbia law for control of narcotics into conformity with the law operating in most States was approved at a hearing May 12th, by a special sub-committee of the House District Committee composed of Representatives Schulte, Indiana; Wood of Missouri; and Cole of New York.

### DEPARTMENT OF PHARMACY, ALABAMA POLYTECHNIC INSTITUTE.

The Business Conference held at Auburn, Ala., April 15th, was a success and it is contemplated to hold these meetings annually. They afford a means of discussing various problems of the pharmacist. Professor George Hargreaves presided at the sessions and Dr. Townes R. Leigh was the principal speaker on the subject, "The Pharmacopœia of the United States, Its Development and Service."

### AMERICAN CHEMICAL SOCIETY.

The Council of the American Chemical Society at its meeting in Kansas City considered the subject of the teaching of chemistry in high schools. Another resolution adopted relates to the creating of standards for instructors in educational institutions offering instruction in chemistry.

### ILLINOIS PHARMACEUTICAL ASSOCIATION.

Illinois Pharmaceutical Association held an interesting and successful meeting at Springfield, May 11th to 13th. About 500 were in attendance. Among the papers of the meeting were those on U. S. P. and N. F. by O. U. Sisson and R. E. Terry.

The new officers are: *President*, Frank M Hewitt, Carbondale; *First Vice-President*, Joe Allegretti, Chicago; *Second Vice-President*, W. E. Brown, Quincy; *Third Vice-President*, M. J. Kerwin, Joliet; *Secretary*, Joseph J. Shine, Chicago; *Treasurer*, A. W. Reinhardt, Rockford.

A vote of thanks was given to **Lee Mrazek,** who had served without salary during the past year as secretary of the Illinois Fair Trade Committee. On behalf of the Association Governor Horner, of Illinois, presented Mr. Mrazek with a handsome traveling bag. The recipient of the gift is leaving on a European trip.

### THE THIRD GERMAN PHARMACEUTICAL CONGRESS.

The Third German Pharmaceutical Congress was held in Stuttgart, Germany, from June

17th to June 21st. The pharmaceutical fair was opened by Dr. J. Schmid, secretary of the Home office, and Minister of Commerce. Extensive publicity was given to the Congress and also to the section around Stuttgart, depicting the beauties of the Black Forest.

### PUBLICITY FOR PHARMACY.

Quoting a paper by Loyd E. Harris, faculty member of the College of Pharmacy in the University of Oklahoma, before the Sixth District National Association of Boards of Pharmacy:

"The famous quotation, 'All I know is what I read in the papers' can easily be applied to the public's conception of pharmacy. Contrast, if you will, the difference in professional appearance between an advertisement of a cut-rate drug store and the publicity of a physician. The doctor does not pay for the space that he gets, but is given the front page to tell about his professional practice. The drug store space costs real money and everything but pharmacy is put before the reader and with emphasis placed on 'cheap.' The majority of druggists are so busy, under these conditions, trying to keep the front door open that they are unable to practice and keep up their professional knowledge. The busy professional man always has time for each one of his clients, but this class of drug store owners insists upon hasty filling of prescriptions so that the man can get out on the floor again and sell cigarettes at fifteen cents, tax included."

"Members of the State Boards of Pharmacy and faculty members of colleges can do much to promote favorable publicity. The schools can give professional training to those entering pharmacy, but it is up to the board members and to our organizations to make and enforce the laws and conditions that will enable them to put this training into practice and keep our profession before the world in a favorable light."

### GRADUATES OF PHARMACY IN JAPAN.

About 2000 students were graduated from pharmacy colleges in Japan this spring. This is about ten per cent of the present number of pharmacists in the country.

## LEGAL AND LEGISLATIVE.

### FOOD, DRUG AND COSMETIC BILL REPORTED.

On May 22nd the House Committee on Interstate and Foreign Commerce reported a substitute for the Copeland bill, S. 5, passed the Senate last year.

Quoting *Bookmeyer Bulletin* in part: The report is No. 2755. "Under the bill reported false advertising of food, drugs, services and cosmetics is brought under regulation by the Secretary of Agriculture and the Federal Trade Commission. The adulteration and misbranding of cosmetics is prohibited. Therapeutic devices are brought under control. Drugs intended for diagnosing illness, or for remedying under-weight or over-weight are subject to regulation. Foods that are dangerous because of naturally contained poisons rather than added poisons are brought under regulation. The addition of poisons to foods is prohibited except where such addition is necessary or cannot be avoided, and in such cases tolerances are provided limiting the amount of added poison to the extent necessary to safeguard the public health. Definitions and standards of identity are provided under which the integrity of food products can be effectively maintained. Informative labeling of foods as to quality and composition is required. The distinctive name proviso of the present law is eliminated. Authority is provided for inspection of factories making interstate shipments. Increased penalties are provided for violations. Multiple seizures would be permitted in cases where the Secretary of Agriculture had probable cause to believe that the misbranding was in a material respect false, misleading or fraudulent. The provision for removal for trial to the jurisdiction of the claimant's residence was changed to permit removal to any district adjacent to the district of the claimant's principal place of business, or to any other district which may be agreed upon by the parties. A special rule will be asked for, fixing a time for consideration and final passage of the bill and limiting debate."

One of the major changes made in the senate bill by the house committee is the transferring of advertising control from the Food and Drug Administration to the Federal Trade Commission.

An amendment requires the Food and Drug Administration to give a manufacturer an official sample of a seized article prior to court trial.

Closing of the May issue of the JOURNAL does not permit discussion of the variation clause provision and other important questions at this time.

## NARCOTICS NOT UNDER SECRET SERVICE.

Representative Robert L. Doughton, of North Carolina, introduced a new bill (H. R. 12556), passed by the House, which provides for the reorganization of the Secret Service, with some modifications. The important feature about the new bill is that it does not affect the Bureau of Narcotics, which continues as at present. It transfers to the Secret Service the enforcement division of the Alcohol Tax Unit and the customs agency service of the Bureau of Customs.

## TYDINGS BILL.

The Tydings-Dies Fair Trade Enabling Act has been reported to the Senate. Favorable action was taken by the Senate Judiciary Committee. The bill has passed.

## ROBINSON-PATMAN BILL.

Chairman Hatton W. Sumners, Wright-Patman, presented arguments in favor of the granting of the special rule calling for early action on the Robinson-Patman Bill. It was approved by the House on May 28th.

## NEW JERSEY FAIR TRADE ACT.

Vice-Chancellor Alfred A. Stein in an opinion filed at Trenton, ruled that the fair trade law is in violation of both the State and Federal constitutions. It is stated that there will be an appeal from the decision.

**Stanley B. Simpson,** Vice-President of Meyer Brothers Drug Company and editor of *Meyer Druggist*, has celebrated the 59th anniversary of his connection with the firm.

**Raoul D. Keim,** Vice-President of E. R. Squibb & Sons, was given a dinner on May 27th, by friends, prior to leaving on a 3-months' vacation abroad.

**Conference Pharmaceutical Association Secretaries.**—*President*, J. W. Slocum, Indianola, Io.; *First Vice-President*, Roy S. Warnack, Los Angeles, Calif.; *Second Vice-President*, Wm. B. Day, Chicago, Ill.; *Secretary-Treasurer*, Carl G. A. Harring, 20 Glen Road, Newton Center, Mass.; *Members of the Executive Committee*, F. V. McCullough, New Albany, Ind.; R. C. Wilson, Athens, Ga.; J. Lester Hayman, Morgantown, W. Va.; Dennis E. Murphy, Cincinnati, Ohio. *Place of Meeting*, Dallas, Texas. *Time*, August 24–29, 1936.

**Conference of Pharmaceutical Law Enforcement Officials.**—*Chairman*, R. L. Swain, 2411 N. Charles St., Baltimore, Md.; *Secretary-Treasurer*, M. N. Ford, New State Office Building, Room G-18, Columbus, Ohio; *Delegate to the House of Delegates*, Fred Schaefer, Brooklyn, N. Y.; *Place of Meeting*, Dallas, Texas. *Time*, August 24–29, 1936.

**International Pharmaceutical Federation.**—*President*, Dr. J. J. Hofman, La Haye; *Secretary General*, Dr. T. Potjewijd, Leyden; *Secretary*, Oscar Van Schoor, Anvers.

## OFFICERS OF AMERICAN DRUG MANUFACTURERS ASSOCIATION

The following officers were elected by the American Drug Manufacturers Association: *President*, A. C. Boylston, St. Louis, Mo.; *First Vice-President*, Oscar W. Smith, Detroit, Mich.; *Second Vice-President*, Dr. L. N. Upjohn, Kalamazoo, Mich.; *Third Vice-President*, S. DeWitt Clough, N. Chicago, Ill.; *Treasurer*, R. Lincoln McNeil, Philadelphia, Pa.; *Executive Vice-President and Secretary*, Carson P. Frailey, Albee Bldg., Washington, D. C.; *General Counsel*, Horace W. Bigelow, Detroit, Mich. *Members of the Executive Committee:* Frederick S. Stearns, Detroit, Mich.; George W. Merck, Rahway, N. J.; John G. Searle, Chicago, Ill.; Carleton H. Palmer, New York City; A. Homer Smith, Philadelphia, Pa.

## OFFICERS OF PROPRIETARY ASSOCIATION.

The following were elected officers at the annual meeting of the Proprietary Association, held in New York City: *President*, Frank A. Blair: *First Vice-President*, Henry P. Bristol; *Second Vice-President*, E. K. Hyde, Buffalo; *Third Vice-President*, J. H. Howe, St. Louis; *Secretary-Treasurer*, Charles P. Tyrrell, Syracuse. Alvin G. Brush and Fred E. Rathburn were elected members of the *Executive Committee*.

## BOOK NOTICES AND REVIEWS.

*Die Fermente und ihre Wirkungen.* (Enzymes and Their Action). Supplement. Lieferung 1 (Bd. I, Specieller Teil, Hauptteil 1 VII–XV). By PROF. CARL OPPENHEIMER, Dr. Phil. et Med. W. Junk Verlag, Scheveningsche Weg 74, The Hague, Holland, 1935. 160 pp. 17 figs. 20.5 x 28 cm. Price $6.80. Lieferung 2 and 3 have recently come to hand, same price.

The author is an outstanding authority on the subject; the work contains correlated information gathered from literature in the field and constitutes valuable sources for references to literature.

Many reviews have appeared in publications largely concerned with the subject and all of them give expression to the work as an international treatise. The *British Medical Journal* states that Professor Oppenheimer is generally recognized as a leading authority; The *Chemical Trade Journal* gives a like credit; *Le Cuir Technique* refers to its comprehensiveness; Swiss, Swedish and German reviews are appreciative of the value of the work rendered by the author.

*Magische Gifte* (*Magic Poisons*) *Rausch und Betäubungsmittel der Neuen Welt.* (*Intoxicants and Narcotics of the New World.*) By PROF. VIKTOR A. REKO, member of the Academy of Sciences, Mexico. 167 pages, cloth, RM. 6.40. (Price outside of Germany and Switzerland 25% additional.) Publishers, Ferdinand Enke Verlag, Stuttgart W, Germany.

The author has presented an interesting book on the use of narcotics, etc., largely by those who use drugs of the kind described, in sections where they have no home ties and are tempted by others who have ventured into wrong-doing. The mystery, secrecy, excitement and surrounding associations, together with a desire to try out the narcotic, leads to a first misstep and to get rid of the effect by the advice of an associate leads to another misuse and brings the person nearer to addiction. Superstition and misinformation are factors. Many of those who go through these experiences follow the sea and become acquainted with life at various ports, and the use of habit formers. The book deals with these subjects interestingly, and local adventures are brought into the chapters.

The subjects are considered under twelve divisions with an introductory in which there is a general discussion. 1. Ololiuqui—Eine Pflanze, die hypnotisieren kann. 2. Peyotl—Ein Kaktus, der Gespenster sehen lässt. 3. Marihuana—Der mexikanische Haschisch. 4. Toloachi—Ein rauchbares Aphrodisiakum. 5. Ayahuasca—Der Trank der grauenhaften Träume. 6. Colorines—Das Geheimnis der roten Bohnen. 7. Sinicuichi—Der vergeblich machende Zaubertrank. 8. Cotztic-Zapote—Eine taumelnd machende Frucht. 9. Nanácatl—Der Irrsinnspilz. 10. Xomil-Xihuite—Der gläserne Sarg. 11. Camotillo—Eine Knolle, die den Todestag voraussagt. 12. Cohombrillo—Das erlösende Katermittel.

The article by H. H. Rusby on the "The Aboriginal uses of Caapi," JOURNAL of December 1923, explains the ceremonials with Ayahusca. Other names will be recognized and the effects indicated are readily translated.

*Prescription Writing and Formulary:* The Art of Prescribing. By CHARLES SOLOMON, M.D., Assistant Clinical Professor of Medicine, Long Island College of Medicine. With a foreword by Lewellys F. Barker, M.D. Cloth. Price, $4.00. Pp. 351, with 32 illustrations. Philadelphia; Publishers: J. B. Lippincott Company, Philadelphia.

The knowledge and skill requisite to prescription writing is an important part of any physician's preparation for the practice of medicine. Individualization of treatment can be practiced only by those familiar with it. The author of this book has prepared a treatise that should fulfil the needs of practicing physicians; it is simple and written in a well organized and lucid manner and the data are in accord with accepted medical practice and therapeutics. The book is unusually complete for its size and bears the mark of careful editing. The formulary is refreshing in its simplicity, avoidance of polypharmacy and preference of official (U. S. P. and N. F.) preparations. The medical student and young practitioner of medicine will welcome this book, and all who are charged with the responsibility of prescription writing can glean much from reading it.

*Die Harze.* A. TSCHIRCH and ERICK STOCK. Third revised edition of A. Tschirch, Die Harze und die Harzebehälter. Band II, Hälfte 2, Teil 1. 544 pages, 173 figures. Gebrüder Borntraeger, Berlin, 1935. Price 54 marks; bound 58 marks. This will serve as an announcement of a work which brings up-to-date information on the subject. The senior

author is our honorary member Professor Dr. Alexander Tschirch, director of the Pharmaceutical Institute of the University of Berne, Switzerland.

*Handbuch Der Pharmakognosie.* Zweite Erweiterte Auflage by A. Tschirch. The issue has been received from Verlag von Bernard Tauchnitz, Leipzig (Lieferung 18). Further reference will be made to this valuable work in a later issue of the JOURNAL.

## NOTICE TO CONTRIBUTORS TO THE JOURNAL AMERICAN PHARMACEUTICAL ASSOCIATION.

The following notice has been prepared from comments received from members of the Board of Review of Papers and of the Publication Committee.

Manuscripts should be sent to Editor E. G. Eberle, 2215 Constitution Ave., N. W., Washington, D. C.

All manuscripts should be typewritten in double spacing on one side of paper $8^1/_2$ x 11 inches, and should be mailed in a flat package—not rolled. The original (*not* carbon) copy should be sent. The original drawings, not photographs of drawings, should accompany the manuscript. Authors should indicate on the manuscript the approximate position of text figures. All drawings should be marked with the author's name and address.

A condensed title running page headline, not to exceed thirty-five letters, should be given on a separate sheet and placed at the beginning of each article.

The method of stating the laboratory in which the work is done should be uniform and placed as a footnote at end of first page, giving Department, School or College. The date when received for publication should be given.

Numerals are used for figures for all definite weights, measurements, percentages, and degrees of temperature (for example: 2 Kg., 1 inch, 20.5 cc., 300° C.). Spell out all indefinite and approximate periods of time and other numerals which are used in a general manner (for example: one hundred years ago, about two and one-half hours, seven times).

Standard abbreviations should be used whenever weights and measures are given in the metric system, *e. g.*, 10 Kg., 2.25 cc., etc. The forms to be used are: cc., Kg., mg., mm., L. and M.

Figures should be numbered from 1 up, beginning with the text-figures (line engravings are always treated as text-figures and should be designed as such) and continuing through the plates. The reduction desired should be clearly indicated on the margin of the drawing. All drawings should be made with India ink, preferably on white tracing paper or cloth. If coördinate paper is used, a blue-lined paper must be chosen. Usually it is desirable to ink in the large squares so that the curves can be more easily read. Lettering should be plain and large enough to reproduce well when the drawing is reduced to the width of a printed page (usually about 4 inches). Photographs intended for half-tone reproduction should be securely mounted with colorless paste.

"Figure" should be spelled out at the beginning of a sentence; elsewhere it is abbreviated to "Fig.;" per cent—2 words.

The expense for a limited number of figures and plates will be borne by the JOURNAL; expense for cuts in excess of this number must be defrayed by the author.

References to the literature cited should be grouped at the end of the manuscript under the *References*. The citations should be numbered consecutively in the order of their appearance (their location in the text should be indicated by full-sized figures included in parentheses). The sequence followed in the citations should be: Author's name (with initials), name of publication, volume number, page number and the date in parentheses. Abbreviations for journals should conform to the style of *Chemical Abstracts*, published by the American Chemical Society.

(1) Author, A. Y., *Am. J. Physiol.*, 79, 289 (1927).

Papers presented at the Sections of the AMERICAN PHARMACEUTICAL ASSOCIATION's annual meeting become the property of the Association and may at the discretion of the Editor be published in the JOURNAL. Papers presented at these Sections may be published in other periodicals only after the release of the papers by the Board of Review of Papers of the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

The Editor will appreciate comments from Board of Review and Committee on Publication, members, authors and others interested.